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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

PHS 2002-1

SOLICITATION OF

THE PUBLIC HEALTH SERVICE

FOR

SMALL BUSINESS INNOVATION RESEARCH

CONTRACT PROPOSALS

PROPOSAL RECEIPT DATE

NOVEMBER 9, 2001

Internet: http://grants.nih.gov/grants/funding/sbir.htm

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The Appendices noted above are in Adobe Acrobat Reader fillable format.

NOTE: Other software packages for completing these applications may be available from other sources; however, it is essential that the type size and format specifications are met or the application will be returned without review.

DISCLAIMER: Reference to these software packages neither constitutes nor should be inferred to be an endorsement or recommendation of any product, service, or enterprise by the National Institutes of Health, any other agency of the United States Government, or any employee of the United States Government. No warranties are stated or implied.

U. S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

SOLICITATION OF THE PUBLIC HEALTH SERVICE FOR SMALL BUSINESS INNOVATION RESEARCH (SBIR) CONTRACT PROPOSALS

I. GENERAL PROGRAM DESCRIPTION

The Small Business Innovation Research Program recently was reauthorized by the enactment of the Small Business Reauthorization Act of 2000, (Public Law 106-554. The Public Health Service (PHS), Department of Health and Human Services (HHS), and certain other Federal agencies must reserve 2.5 percent of their current fiscal year extramural budgets for research or research and development (R/R&D) for a Small Business Innovation Research (SBIR) program. The objectives of the SBIR Program include stimulating technological innovation in the private sector, strengthening the role of small business in meeting Federal R/R&D needs, increasing private sector commercialization of innovations developed through Federal SBIR R&D, increasing small business participation in Federal R&D, and fostering and encouraging participation by socially and economically disadvantaged small business concerns and women-owned small business concerns in the SBIR program.

The SBIR program consists of three separate phases:

Phase I: Feasibility
$100,000
6 months

The objective of Phase I is to determine the scientific or technical feasibility and commercial merit of the proposed research or R&D efforts and the quality of performance of the small business concern, prior to providing further Federal support in Phase II. Phase I awards normally may not exceed $100,000 for direct costs, indirect costs, and profit (fixed fee) for a period normally not to exceed 6 months.

Phase II: Full R/R&D Effort
$750,000
2 years

The objective of Phase II is to continue the research or R&D efforts initiated in Phase I. Funding shall be based on the results of Phase I and the scientific and technical merit and commercial potential of the Phase II proposal. Phase II awards normally may not exceed $750,000 for direct costs, indirect costs, and negotiated fees for a period normally not to exceed two years. That is, generally, a two-year Phase II project may not cost more than $750,000 for that project. *Phase II proposals may only be submitted upon the request of the Contracting Officer, if not submitted concurrently with the initial Phase I proposal under the Fast-Track procedure (described in Section V.) Only one Phase II award may result from a single Phase I SBIR contract.*

Phase III: Commercialization stage without SBIR funds

The objective of Phase III, where appropriate, is for the small business concern to pursue with non-Federal funds the commercialization objectives resulting from the results of the research or R&D funded in Phases I and II. In some Federal agencies, Phase III may involve follow-on, non-SBIR funded R&D or production contracts for products or processes intended for use by the U.S. Government.

Please direct questions of a general nature about the NIH SBIR Program to:

Ms. Jo Anne Goodnight
NIH SBIR/STTR Program Coordinator
6701 Rockledge Drive
Rockledge II, Room 6186
Bethesda, MD 20892-7911
Phone: (301) 435-2688 Fax: (301) 480-0146
E-mail: jg128w@nih.gov

A. PURPOSE OF SOLICITATION

The purpose of this Solicitation is to *invite Phase I contract proposals from small business* concerns that have the expertise to contribute to the mission of the awarding components identified below and to provide the opportunity for the submission of Phase II contract

proposals concurrently with Phase I (see specific topics listed in Section XII and identified as accepting Fast-Track proposals.)

Included are instructions for offerors to prepare contract proposals, a description of the proposal review process, and some conditions of a contract award. *Contract proposals will be accepted only if they respond specifically to a research topic within this Solicitation (see Section XII "Research Topics.")* Otherwise, proposals will be returned to the offeror(s) without evaluation.

B. AWARDING COMPONENTS

The following awarding components of the PHS are participating in this SBIR Solicitation for Contract Proposals.

National Institutes of Health (NIH)

- National Institute on Alcohol Abuse and Alcoholism (NIAAA)
- National Cancer Institute (NCI)
- National Institute of Child Health and Human Development (NICHD)
- National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)
- National Institute on Drug Abuse (NIDA)
- National Institute of Environmental Health Sciences (NIEHS)
- National Institute of Mental Health (NIMH)
- National Institute of Neurological Disorders and Stroke (NINDS)

Centers for Disease Control and Prevention (CDC)

- National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP)
- National Center for Environmental Health (NCEH)
- National Center for HIV, STD, and TB Prevention (NCHSTP)
- National Center for Infectious Diseases (NCID)
- National Center for Injury Prevention and Control (NCIPC)

To apply for an SBIR grant rather than a contract, use the *Omnibus Solicitation of the Public Health Service for Small Business Innovation Research Grant Applications*.

C. SBIR PROGRAM ELIGIBILITY

Organizational Criteria: Each organization submitting a proposal under the SBIR program must qualify as a small business concern (defined in Section III.) In determining whether an offeror is a small business concern, an assessment will be made of several factors, including whether or not it is independently owned and operated and whether or not it is an affiliate of a larger organization whose employees, when added to those of the offeror organization, exceed 500. In conducting this assessment, all appropriate factors will be considered, including common ownership, common management, and contractual relationships.

In accordance with 13 CFR 121.3, affiliation exists when "… one concern controls or has the power to control the other … control may be affirmative or negative and it is immaterial whether it is exercised so long as the power to control exists." One of the circumstances that would lead to a finding that an organization is controlling or has the power to control another organization involves sharing common office space and/or employees and/or other facilities (e.g., laboratory space). 13 CFR 121.3 also states that control or the power to control exists when "key employees of one concern organize a new concern … and serve as its officers, directors, principal stockholders, and/or key employees; and one concern is furnishing or will furnish the other concern with subcontracts, financial or technical assistance, and/or other facilities, whether for a fee or otherwise."

Access to special facilities or equipment in another organization is permitted (as in cases where the SBIR awardee has entered into a subcontractual agreement with another institution for a specific, limited portion of the research project). However, *research space*

occupied by an SBIR contractor organization must be space that is available to and under the control of the SBIR contractor for the conduct of its portion of the project. Where there is indication of sharing of common employees, a determination will be made on a case-by-case basis of whether or not such sharing constitutes control or the power to control.

Whenever a proposed SBIR project is to be conducted in facilities other than those of the offeror organization, a letter must be submitted *with* the proposal stating that leasing/rental arrangements have been negotiated for appropriate research space (i.e., space that will be available to and under the control of the SBIR contractor organization).

This letter must be signed by an *authorized official of the organization whose facilities are to be used for the SBIR project.* It also must include a description of the facilities and, if appropriate, equipment that will be leased/rented to the offeror organization.

All SBIR contract proposals will be reviewed with the above considerations in mind. *If it appears that an offeror organization does not meet eligibility requirements, the PHS will request a size determination of the organization from the cognizant Small Business Administration (SBA) regional office. The evaluation of the proposal for scientific merit will be deferred until the SBA provides a determination*.

Principal Investigator Criteria. The primary employment of the principal investigator must be with the offeror at the time of contract award and during the conduct of the proposed project. PHS policy defines a principal investigator as the single individual designated in the contract proposal with responsibility for the scientific and technical direction of the project. Primary employment means that *more than one half of the principal investigator's time* is spent in the employ of the small business concern. *Primary employment with a small business concern precludes full-time employment at another organization*.

In the event that the principal investigator: (1) is a less-than-full-time employee of the small business, (2) is concurrently employed by another organization, or (3) gives the appearance of being concurrently employed by another organization, whether for a paid or unpaid position, at the time of submission of the proposal, *it is essential that documentation be submitted with the proposal to verify his/her eligibility*. If the principal investigator also is employed or appears to be employed by an organization other than the offeror organization (e.g., a university, a nonprofit research institute, or another company), a letter must be provided by the *non-offeror organization* confirming that the principal investigator will, if awarded an SBIR contract, become a less-than-half-time employee of such organization and will remain so for the duration of the SBIR project. If the principal investigator is employed by a university, the Dean's Office must provide such a letter. If the principal investigator is employed by another for-profit organization, the corporate official must sign the letter. This documentation is required for every proposal that is submitted, even one that is a revision of a previously submitted proposal.

Performance Site Criteria. For both Phase I and Phase II, the research or R&D project activity *must be performed in its entirety in the United States (see Section III. Definitions)*.

Market Research. *The PHS will not support any market research under its SBIR program*. Neither will it support studies of the literature that will lead to a new or expanded statement of work. Literature searches where the commercial product is a database are acceptable. For purposes of the SBIR program, “market research” is the systematic gathering, recording, computing, and analyzing of data about problems relating to the sale and distribution of the subject of the research project. It includes various types of research, such as the size of potential market and potential sales volume, the identification of consumers most apt to purchase the products, and the advertising media most likely to stimulate their purchases. However, “market research” does not include activities under a research plan or protocol that require a survey of the public as part of the objective of the project to determine the impact of the subject of the research on the behavior of individuals.

II. AGENCY CONTACT FOR INFORMATION

Questions on the administration of the PHS SBIR contract program should be directed to the contracting officers listed in Section X. Contracting Officers and Addresses for Mailing and Delivery of Proposals.

The PHS SBIR Contract Solicitation ***is available in electronic PDF format*** on the NIH's "Small Business Funding Opportunities" home page at http://grants.nih.gov/grants/ funding/sbir.htm Printed copies of the Solicitation will not be distributed. The Table of Contents includes direct links and cross-references to specific sections of the document. Text searches are possible using the "binocular" icon. The Phase I and Phase II forms have been modified to enable the fields to be filled in directly using Adobe Acrobat Reader software, which is free.

HELP AND INSTRUCTIONS are available for printing and viewing Acrobat files. Information on Fillable PDF Forms is also available.

NOTE: Other software packages for completing these applications may be available from other sources; however, it is essential that the type size and format specifications are met or the application will be returned without review.

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III. DEFINITIONS

Clinical Research. NIH defines human clinical research as: **(1)** Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are *in vitro* studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes: (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, or (d) development of new technologies. **(2)** Epidemiologic and behavioral studies. **(3)** Outcomes research and health services research. Note: Studies falling under Exemption 4 for human subjects research are not considered clinical research by this definition.

Commercialization. The process of developing markets and producing and delivering products for sale (whether by the originating party or by others); as used here, commercialization includes both government and private sector markets.

Contract. An award instrument establishing a binding legal procurement relationship between a funding agency and the recipient, obligating the latter to furnish an end product or service and binding the agency to provide payment therefore.

Essentially Equivalent Work. This term is meant to identify "scientific overlap," which occurs when: (1) substantially the same research is proposed for funding in more than one proposal (contract proposal or grant application) submitted to the same Federal agency; OR (2) substantially the same research is submitted to two or more different Federal agencies for review and funding consideration; OR (3) a specific research objective and the research design for accomplishing that objective are the same or closely related in two or more proposals or awards, regardless of the funding source.

Funding Agreement. Any contract, grant, cooperative agreement, or other transaction entered into between and Federal agency and any small business concern for the performance of experimental, developmental, or research work funded in whole or in part by the Federal Government.

Innovation. Something new or improved, including research for: (1) development for new technologies, (2) refinement of existing technologies, or (3) development of new applications for existing technologies. For purposes of PHS programs, an example of "innovation" would be new medical or biological products, for improved value, efficiency, or costs.

Key Personnel Engaged on Project. This term is meant to identify those individuals who contribute in a substantive way to the scientific development or execution of the project, whether or not salaries are requested.

Prototype. A model of something to be further developed that includes designs, protocols, questionnaires, software, devices, etc.

Research or Research and Development (R/R&D). Any activity that is:

1. A systematic, intensive study directed toward greater knowledge or understanding of the subject studied.
2. A systematic study directed specifically toward applying new knowledge to meet a recognized need.
3. A systematic application of knowledge toward the production of useful materials, devices, and systems or methods, including design, development, and improvement of prototypes and new processes to meet specific requirements.

Small Business Concern. A small business concern is one that, at the time of award of Phase I and Phase II, meets all of the following criteria:

1. Is independently owned and operated, is not dominant in the field of operation in which it is proposing, has its principal place of business located in the United States, and is organized for profit;
2. Is at least 51 percent owned, or in the case of a publicly owned business, at least 51 percent of its voting stock is owned by United States citizens or lawfully admitted permanent resident aliens;
3. Has, including its affiliates, a *number of employees not exceeding 500*, and meets the other regulatory requirements found in 13 CFR Part 121. Business concerns, other than investment companies licensed, or state development companies qualifying under the Small Business Investment Act of 1958, 15 U.S.C. 661, *et seq.,* are affiliates of one another when either directly or indirectly:
    a. One concern controls or has the power to control the other; or
    b. A third party or parties controls or has the power to control both.

    Control can be exercised through common ownership, common management, and contractual relationships. The term "affiliates" is defined in greater detail in 13 CFR 121.3-2(a). The term "number of employees" is defined in 13 CFR 121.3-2(t). *Business concerns include, but are not limited to, any individual (sole proprietorship), partnership, corporation, joint venture, association, or cooperative*.

Joint Ventures or Limited Partnerships. Joint ventures and limited partnerships are eligible provided the entity created qualifies as a small business concern as defined in this Solicitation.

Socially and Economically Disadvantaged Individual. A member of any of the following groups:

- Black Americans
- Hispanic Americans
- Native Americans
- Asian-Pacific Americans
- Subcontinent Asian Americans
- Other groups designated from time to time by SBA to be socially disadvantaged
- Any other individual found to be socially and economically disadvantaged by SBA pursuant to Section 8(a) of the Small Business Act,15 U.S.C. 637(a)

Socially and Economically Disadvantaged Small Business Concern. A socially and economically disadvantaged small business concern:

1. Is one that is at least 51 percent owned by: (a) an Indian tribe or a native Hawaiian organization, or (b) one or more socially and economically disadvantaged individuals; and
2. Whose management and daily business operations are controlled by one or more socially and economically disadvantaged individuals.

Subcontract. Any agreement, other than one involving an employer-employee relationship, entered into by a Federal Government prime contractor calling for supplies or services required solely for the performance of the prime contract or another subcontract.

United States. The 50 states, the territories and possessions of the U.S., the Commonwealth of Puerto Rico, the Trust Territory of the Pacific Islands, and the District of Columbia.

Woman-Owned Small Business Concern. A small business concern that is at least 51 percent owned by a woman or women who also

control and operate it. "Control" in this context means exercising the power to make policy decisions. "Operate" in this context means being actively involved in the day-to-day management.

IV. PHASE I PROPOSAL PREPARATION INSTRUCTIONS AND REQUIREMENTS

A. LIMITATIONS ON LENGTH OF PROPOSAL

SBIR Phase I proposals shall not exceed a total of *25 single-spaced pages*, including the cover sheet, cost breakdown, and all enclosures or attachments. *Pages should be of* standard size (8 l/2" X 11*"),* and the font should be no smaller than 10-point. *Excluded* from the 25-page limitation are cover letters, letters of commitment from collaborators and consultants and letters to determine eligibility. Unless specifically solicited by a Contracting Officer, no other appendices may be submitted, and if submitted, they will not be considered in the evaluation of scientific and technical merit.

B. PROPOSAL COVER SHEET

Complete the form identified as Appendix A and use it as the first page of the proposal. *No other cover sheet should be used*.

- ***Topic Number.*** Provide the appropriate numerical designator of the research topic for which your proposal is being submitted. If your proposal is responsive to a subtopic, provide both the topic and subtopic numbers. (A numerical or alphabetical designator precedes each topic and subtopic.)

- ***Project Title.*** Select a title that reflects the substance of the project. Do not use the title of the topic that appears in the Solicitation.

C. ABSTRACT OF RESEARCH PLAN

Complete the form identified as Appendix B, and insert it as the second page of each proposal. Abstracts of successful proposals will be published by NIH and, therefore, should not contain proprietary information. The abstract should include a brief description of the problem or opportunity, specific aims, and a description of the effort. Summarize anticipated results and potential commercial applications of the proposed research.

D. RESEARCH PLAN

Any research proposal involving the collection of information, such as surveys or interviews, of more than nine respondents will require clearance by the U.S. Office of Management and Budget. Therefore, it is not practical to propose such an activity for Phase I, which normally has only a six-month duration.

Beginning on page three of the proposal, discuss in the order indicated the following elements:

1. ***Identification and Significance of the Problem or Opportunity.*** Provide a clear statement of the specific technical problem or opportunity addressed.

2. ***Technical Objectives.*** State the specific objectives of the Phase I effort, including the technical questions it will try to answer to determine the feasibility of the proposed approach.

3. ***Work Plan.*** Provide a detailed plan for the R&D to be carried out, including the experimental design, procedures, and protocols to be used. Address the objectives and the questions stated in *Item 2* above. Discuss in detail the methods to be used to achieve each objective or task.

4. ***Related Research or R&D.*** Describe significant research or R&D that is directly related to the proposal, including any conducted by the principal investigator/project manager or by the proposing firm. Describe how it relates to the proposed effort and any planned coordination with outside sources. *The principal investigator/project manager must persuade reviewers of his or her awareness of recent significant research or R&D conducted by others in the same scientific field*.

5. ***Relationship with Future R&D.***

   a. State the results expected from the proposed approach.

b. Discuss the significance of the Phase I effort in providing a foundation for the Phase II R/R&D effort.

6. ***Potential Commercial Applications.*** Describe why the proposed project appears to have potential commercial applications, and whether and by what means the proposed project appears to have potential use by the Federal Government.

7. ***Key Personnel and Bibliography of Directly Related Work.*** Identify key personnel, including their directly related education, experience, and bibliographic information. Where vitae are extensive, focus on summaries of the most relevant experience or publications. *Provide dates and places of employment* and some information about the nature of each position or professional experience. Curriculum vitae must identify the current or most recent position.

8. ***Salary Rate Limitation.*** Beginning with the HHS Appropriations Act of Fiscal Year (FY) 1990, direct salary rate limitations have been placed on the NIH contracts that support the NIH Extramural R&D activities. Direct salary is exclusive of overhead, fringe benefits, and general and administrative expenses. The FY 2001 HHS Appropriations Act limited the direct salary rate using FY 2001 funds to Executive Level II, which is currently $161,200 per year. It is anticipated that this same limit will apply in FY 2002.

9. ***Consultants.*** Involvement of consultants in the planning and/or research stages of the project is permitted. However, such use must be described in detail and supported by appropriate letters from each individual confirming his/her role in the project.

10. ***Facilities and Equipment.*** Indicate where the proposed research will be conducted. *One of the performance sites must be the offeror organization*. Describe the facilities to be used; identify the location; and briefly indicate their capacities, pertinent capabilities, relative proximity, and extent of availability to the project. Include clinical, computer, and office facilities of the offeror and those of any other performance sites to be used in the project.

    List the most important equipment items already available for this project, noting location and pertinent capabilities of each.

    Any equipment and products purchased with Government funds shall be American-made, to the extent possible.

    Title to Equipment. Title to equipment purchased with Government funding by the SBIR awardee in relation to project performance vests upon acquisition in the Federal Government. However, the Government may transfer such title to an SBIR awardee upon expiration of the project where the transfer would be more cost-effective than recovery of the property.

E. CURRENT AWARDS AND PENDING PROPOSALS/APPLICATIONS

As the PHS uses both contracts and grants in its SBIR program, a small business concern may not submit both a contract proposal and a grant application for essentially the same project to the same or different awarding component(s) of the PHS. The only exception would be the submission of a grant application after a contract proposal has been evaluated and is no longer being considered for award.

While it is permissible, with proposal notification, to submit identical proposals or proposals containing a significant amount of essentially equivalent work (as defined in this Solicitation) for consideration under numerous Federal program solicitations, it is unlawful to enter into contracts or grants requiring essentially equivalent effort.

If there is any question concerning this, it must be disclosed to the soliciting agency or agencies before award.

If a firm elects to submit identical proposals or proposals containing a significant amount of essentially equivalent work under other Federal program solicitations, include a statement in each such proposal indicating the information requested in items 1-10 set forth below.

In addition, provide the information requested in items 1-10 on (a) active funding through contracts, grants, and cooperative agreements from public or private sponsors; (b) contract proposals and grant and cooperative agreement applications pending review or funding; and (c)

contract proposals and grant and cooperative agreement applications about to be submitted.

1. Name and address of the funding source.
2. Type of award (contract, grant, cooperative agreement) and identifying number.
3. Title of research project.
4. Name and title of principal investigator or project manager.
5. Hours per week on the project by the principal investigator or project manager.
6. Annual costs proposed or awarded.
7. Entire period of support.
8. Date of proposal/application submission or date of award.
9. Title, number, and date of solicitations under which proposals or applications were submitted or awards received.
10. The specific applicable research topic for each SBIR proposal or application submitted or award received. *Specifically identify those projects that are SBIR*.

F. PRIOR SBIR PHASE II AWARDS

If the small business concern has received more than 15 Phase II awards in the prior 5 fiscal years, submit name of awarding agency, date of award, funding agreement number, amount, topic or subtopic title, follow-on agreement amount, source, and date of commitment and current commercialization status for each Phase II. This required proposal information will not be counted toward the proposal page limitations.

G. PROPOSED COST BREAKDOWN

Complete the form identified as Appendix C (Contract Pricing Proposal). The cost breakdown should appear as the last section of the proposal. *If some items on this form do not apply to the proposed project, they need not be completed*.

- Under "Government Solicitation No.," enter "PHS 2002-1."
- If supplies are proposed, provide the quantities and the price per unit.
- Under "Direct Labor," *list all key personnel by name*. Support personnel may be consolidated into categories or labor classes, e.g., research assistants or data processing clerks.
- If travel is proposed, provide the following details on "Exhibit A – Supporting Schedule": destination(s); duration of trip(s); number of travelers; and cost per trip, broken down by cost elements, e.g., airfare, lodging, and meals.
- If consultants are proposed, provide name(s), rate(s), and number of hours/days.
- If a subcontract is proposed, provide the same type of detailed cost breakdown as required for Appendix C. *Also provide a copy of the subcontractual agreement*.
- Use "Exhibit A – Supporting Schedule" to itemize and justify all major cost elements.

Normally, at least two-thirds or 67% of the entire research or analytical effort must be carried out by the offeror, i.e., subcontracts for portions of the scientific/technical effort and consultant fees normally may not exceed 33% of the total cost breakdown.

H. STREAMLINING THE CONTRACTING PROCESS

With the Federal Acquisition Streamlining Act of 1994 and the Federal Acquisition Reform Act of 1996, a number of terms and conditions that previously applied to contracts under $100,000 are no longer applicable. Under the SBIR program, Phase I awards, which normally may not exceed $100,000, will reflect the streamlined contract document.

The NIH has initiated special *"just in time" procedures* that are designed to reduce the administrative burden on offerors without compromising the information needed during the initial evaluation of proposals. Certain documents that would previously have been required for submission with the Phase II proposal will be requested at a later stage in the evaluation process. The following documentation is part of the "just in time" procedures and offerors who elect to submit proposals under the *"Fast-Track" initiative* below are not required to submit this documentation with their initial Phase II business proposal:

- ***Travel Policy.*** The offeror's written travel policy.
- ***Annual Financial Report.*** The offeror's most recent annual financial report.
- ***Total Compensation Plan.*** Salary and fringe benefits of professional employees under service contracts.
- ***Data Substantiating the Costs and Prices Proposed.*** That is, payroll documentation, vendor quotes, invoice prices, etc.

I. REQUIRED EDUCATION IN THE PROTECTION OF HUMAN RESEARCH PARTICIPANTS

NIH requires education on the protection of human research participants for all individuals identified as "key personnel" before funds are awarded for contract proposals involving human subjects. For information relating to this requirement, see the following notice (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html), which was published June 5, 2000 in the *NIH Guide for Grants and Contracts*. Prior to award, the selected contractor will be required to provide a description of education completed in the protection of human subjects for all key personnel. While NIH does not endorse programs, there are curricula available that can provide guidance or that can be modified to provide training in this area. See http://helix.nih.gov:8001/ohsr/newcbt for computer-based training developed for NIH that can be downloaded at no charge and modified for use. For information on facilitating education and developing curricula, see http://www.nih.gov/sigs/bioethics.

J. INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH

It is NIH policy that women and members of minority groups and their subpopulations must be included in all NIH-supported biomedical and behavioral research projects involving human subjects (see http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-048.html) unless a clear and compelling rationale shows that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. Exclusion under other circumstances may be based on a compelling rationale and justification. Cost is not an acceptable reason for exclusion except when the study would duplicate data from other sources. Women of childbearing potential should not be routinely excluded from participation in clinical research. This policy applies to research subjects of all ages.

The inclusion of women and members of minority groups and their subpopulations must be addressed in developing a research design appropriate to the scientific objectives of the study. Describe the composition of the proposed study population in terms of gender and racial/ethnic group, and provide a rationale for selection of such subjects. Include a description of the proposed outreach programs for recruiting women and minorities as participants.

All research projects involving human subjects are subject to the policy, whether or not they are exempt from human subject protections and Institutional Review Board (IRB) review requirements. All investigators proposing research involving human subjects should read the "NIH Guidelines On the Inclusion of Women and Minorities as Subjects in Clinical Research", which was published in the *NIH Guide for Grants and Contracts (August 2, 2000.) Investigators may also obtain a copy from the contracting officers found in Section X of this Solicitation.*

K. INCLUSION OF CHILDREN IN RESEARCH INVOLVING HUMAN SUBJECTS

It is NIH policy that children must be included in all human subjects research, including, but not limited to, clinical trials, conducted under a contract funded by the NIH, unless there are scientific or ethical reasons not to include them.

For purposes of this policy, a "child" is defined as an individual under the age of 21 years. Contracts involving human subjects include categories that would otherwise be exempt from the HHS regulations for the Protection of Human Research Subjects (sections 101(b) and 401(b) of 45 CFR 46), such as surveys, evaluation of educational interventions, and studies of existing data or specimens that should include children as participants. This policy applies to both domestic and foreign research contracts.

Inclusion of children as participants in research must be in compliance with all applicable

subparts of 45 CFR 46 as well as other pertinent laws and regulations, whether or not such research is otherwise exempt from 45 CFR 46. Therefore, any proposals must include a description of plans for including children, unless the offeror presents clear and convincing justification for an exclusion. In the technical proposal, the offeror should create a section titled "Participation of Children." Provide either a description of the plans to include children and a rationale for selecting or excluding a specific age range of child, or an explanation of the reason(s) for excluding children as participants in the research.

All investigators proposing research involving human subjects should read the "NIH Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects," which was published in the *NIH Guide for Grants and Contracts* on March 6, 1998, and is available at http://grants.nih.gov/grants/guide/notice-files/not98-024.html

Investigators may also obtain copies from the contracting officers found in Section X of this Solicitation.

L. REQUIREMENT FOR ADEQUATE ASSURANCE OF PROTECTION OF HUMAN SUBJECTS

The HHS regulations for the Protection of Human Subjects, 45 CFR 46 (as amended), provide a systematic means, based on established ethical principles, to safeguard the rights and welfare of individuals who participate as subjects in research activities supported or conducted by the HHS. The requirement is that an approved assurance of compliance with the regulations must be on file with the Office for Human Research Protections (OHRP), DHHS (formerly Office for Protection from Research Risks (OPRR), NIH) before an HHS award can be made.

Neither an Institutional Review Board (IRB) review nor an OHRP-approved Assurance is required at the time the proposal is submitted or at the time that the proposals are peer reviewed.

The review group will consider carefully whether the proposal includes necessary safeguards to protect the rights and welfare of research participants. *No contract award can be made without IRB approval.* Therefore, following NIH peer review and notification of an Institute's decision to proceed with negotiations and funding, the offeror should proceed with IRB review. On request of the awarding component, OHRP will contact the offeror to provide detailed instructions for filing the necessary documents to request a Single Project Assurance (SPA).

The regulations define a "human subject" as a "living individual about whom an investigator (whether professional or student) conducting research obtains: (1) data through intervention or interaction with the individual, or (2) identifiable private information." The regulations extend to the use of human organs, tissue, and body fluids from individually identifiable human subjects as well as to graphic, written, or recorded information derived from individually identifiable human subjects. The use of autopsy materials is governed by applicable state and local law and is not directly regulated by 45 CFR 46 (as amended).

In doubtful cases, prior consultation with the Office for Human Research Protections (OHRP), DHHS, (301) 496-7041, may be of assistance.

Inappropriate designations of the non-involvement of human subjects in an SBIR project may result in delays in the review of a proposal. The OHRP, on behalf of HHS, will make a final determination of whether the proposed activities are covered by the regulations or are in an exempt category, based on the information provided in the proposal.

Any SBIR contract involving human subjects that is awarded as a result of a proposal submitted in response to this Solicitation will include the following clauses:

1. The Contractor agrees that the rights and welfare of human subjects involved in research under this contract shall be protected in accordance with 45 CFR Part 46 (as amended) and with the Contractor's current Assurance of Compliance on file with the Office for Human Research Protections (OHRP), DHHS. The Contractor further agrees to provide certification at least annually that the institutional review board has reviewed and approved the procedures which involve human subjects in accordance with 45 CFR Part 46 (as amended) and the Assurance of Compliance.

2. The Contractor shall bear full responsibility for the performance of all work and services involving the use of human subjects under this contract in a proper manner and as safely as is feasible. The parties hereto agree that the Contractor retains the right to control and direct the performance of all work under this contract. Nothing in this contract shall be deemed to constitute the Contractor or any subcontractor, agent or employee of the Contractor, or any other person, organization, institution, or group of any kind whatsoever, as the agent or employee of the Government. The Contractor agrees that it has entered into this contract and will discharge its obligations, duties, and undertakings and the work pursuant thereto, whether requiring professional judgment or otherwise, as an independent Contractor without imputing liability on the part of the Government for the acts of the Contractor or its employees.

3. If at any time during performance of this contract, the Contracting Officer determines, in consultation with the OHRP, DHHS, that the Contractor is not in compliance with any of the requirements and/or standards stated in paragraphs (1) and (2) above, the Contracting Officer may immediately suspend, in whole or in part, work and further payments under this contract until the Contractor corrects such noncompliance. Notice of the suspension may be communicated by telephone and confirmed in writing.

   If the Contractor fails to complete corrective action within the period of time designated in the Contracting Officer's written notice of suspension, the Contracting Officer may, in consultation with OHRP, DHHS, terminate this contract in whole or in part, and the Contractor's name may be removed from the list of those Contractors with approved Health and Human Services Human Subject Assurances.

M. NEEDLE EXCHANGE

It is anticipated that the HHS Fiscal Year 2002 Appropriations Act will continue a restriction on using contract funds to carry out any program of distributing sterile needles or syringes for the hypodermic injection of any illegal drug.

N. BAN ON HUMAN EMBRYO RESEARCH

It is anticipated that the HHS Fiscal Year 2002 Appropriations Act will continue the ban on funding of human embryo research. Currently, contract funds may not be used for: (1) the creation of a human embryo or embryos for research purposes, or (2) research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero under 45 CFR 46.208(a)(2) and Section 498(b) of the Public Health Service Act (42 U.S.C. 289g(b)). The term “human embryo or embryos” includes any organism, not protected as a human subject under 45 CFR 46 as of the date of the Act, that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes or human diploid cells. Additionally, Federal funds may not be used for cloning of human beings.

O. REQUIREMENT FOR ADEQUATE ASSURANCE OF COMPLIANCE WITH THE PHS POLICY ON HUMANE CARE AND USE OF LABORATORY ANIMALS

The PHS Policy on Humane Care and Use of Laboratory Animal (Policy) establishes a number of requirements in research activities involving live, vertebrate animals. It stipulates that an offeror organization, whether domestic or foreign, bears responsibility for the humane care and use of animals in PHS-supported research activities. The PHS Policy defines “animal” as “any live, vertebrate animal used or intended for use in research, research training, experimentation or biological testing or for related purposes.” An offeror organization proposing to use animals in PHS- supported activities must file a written Animal Welfare Assurance with the Office of Laboratory Animal Welfare (OLAW), NIH. When an offeror proposes research that involves animals, but the offeror does not have an Animal Welfare Assurance on file with OLAW, on request of the awarding component, OLAW will contact the offeror and provide detailed instructions for filing the necessary document.

Neither an Institutional Animal Care and Use Committee (IACUC) nor an OLAW-approved Assurance is required at the time the proposal is submitted.

Institutions having an Assurance with OLAW are encouraged to have an IACUC review before submitting the proposal and should furnish verification of IACUC approval with the proposal. However, an Assured organization may submit the verification of IACUC review after proposal submission but before the Initial Technical Review is initiated. If verification is not received before the Initial Technical Review meeting, the awarding component will not allow the review of the proposal.

No PHS award for research involving animals will be made unless the offeror organization is operating in accord with an approved Animal Welfare Assurance and provides verification that the IACUC has reviewed and approved the proposed activity in accordance with PHS Policy. 48 CFR Part PHS 352 requires that any contract involving live, vertebrate animals, awarded as a result of a proposal submitted in response to this Solicitation include the following clauses:

1. Before undertaking performance of any contract involving research on live, vertebrate animals, the Contractor shall register with the Secretary of Agriculture of the United States in accordance with 7 U.S.C. 2316 and 9 CFR Section 2.30. The Contractor shall furnish evidence of such registration to the Contracting Officer.
2. The Contractor shall acquire animals used in research from a dealer licensed by the Secretary of Agriculture under 7 U.S.C. 2131-2157 and 9 CFR Sections 2.1-2.11, or from a source that is exempt from licensing under those sections.
3. The Contractor agrees that the care and use of any live, vertebrate animals used or intended for use in the performance of this contract will conform with the PHS Policy on Humane Care and Use of Laboratory Animals, the current Animal Welfare Assurance, the Guide for the Care and Use of Laboratory Animals prepared by the Institute of Laboratory Animal Resources, and the pertinent laws and regulations of the United States Department of Agriculture (see 7 U.S.C. 2131 *et seq.* and 9 CFR Subchapter A, Parts 1-3). In case of conflict between standards, the more stringent standard shall be used.
4. If at any time during performance of this contract, the Contracting Officer determines, in consultation with the Office of Laboratory Animal Welfare (OLAW), National Institutes of Health (NIH), that the Contractor is not in compliance with any of the requirements and/or standards stated in paragraphs (1) through (3) above, the Contracting Officer may immediately suspend, in whole or in part, work and further payments under this contract until the Contractor corrects the noncompliance. Notice of the suspension may be communicated by telephone and confirmed in writing. If the Contractor fails to complete corrective action within the period of time designated in the Contracting Officer's written notice of suspension, the Contracting Officer may, in consultation with OLAW, NIH, terminate this contract in whole or in part, and the Contractor's name may be removed from the list of those Contractors with approved Public Health Service Animal Welfare Assurances.

The Contractor may request registration of its facility and a current listing of licensed dealers from the Animal Care Sector Office of the Animal and Plant Health Inspection Service (APHIS), USDA, for the sector in which its research facility is located. The location of the appropriate APHIS Regional Office, as well as information concerning this program, may be obtained by contacting:

Animal Care Staff
USDA/APHIS
4700 River Road, Unit 84
Riverdale, MD 20737
(301) 734-4980

Offerors proposing research that involves live, vertebrate animals will be contacted by OLAW and given detailed instructions on filing a written Animal Welfare Assurance with the PHS.

Offerors are encouraged to visit the OLAW website at http://grants.nih.gov/grants/olaw/olaw.htm for additional information. OLAW may be contacted at the National Institutes of Health at (301) 594-2289.

P. RESEARCH USING HUMAN PLURIPOTENT STEM CELLS

In signing the application Face Page, the duly authorized representative of the applicant organization certifies that if research using human pluripotent stem cells is proposed, the applicant organization will be in compliance with

the National Institutes of Health Guidelines for Research Using Human Pluripotent Stem Cells published in the Federal Register http://www.nih.gov/news/stemcell/stemcellguidelines.htm.

V. "FAST-TRACK" INITIATIVE

(Applicable Only to Proposals Submitted to NIH)

The "Fast-Track" initiative is a parallel review option available to those small business concerns (offeror organizations) whose proposals satisfy additional criteria that enhance the probability of the project's commercial success. This initiative is applicable only to NIH and only if an awarding component indicates it is accepting Fast Track proposals for a particular topic. (Refer to Section XII, "Research Topics," for notation.)

The Fast-Track initiative is an opportunity for small business concerns to submit both a Phase I and Phase II proposal for concurrent peer review. This initiative also has the potential to minimize any funding gap between Phase I and Phase II.

Fast-Track Proposal Process

To identify the proposals as Fast-Track, check the box marked "Yes" next to the words "Fast-Track Proposal" shown on the Phase I Proposal Cover Sheet (Appendix A).

The small business concern must submit both a Phase I and a Phase II proposal for concurrent initial peer review and evaluation. The Fast-Track proposal must consist of the following parts:

1. ***Phase I Proposal.*** Prepared in accordance with Section IV. Phase I Proposal Preparation Instructions and Requirements, and addressing all factors stated in the evaluation criteria (Section VII) for Phase I proposals.
2. ***Phase II Proposal.*** Prepared in accordance with Section VI, Fast-Track Phase II Proposal Preparation Instructions and Requirements and addressing all factors stated in the evaluation criteria (Section VII) for Phase II proposals.
3. ***Product Development Plan.*** A concise document (limited to ten pages), which addresses each of the following areas:
   a. Company information, including size, specialization area(s), products with significant sales, and history of previous Federal and non-Federal funding, regulatory experience, and record of commercializing SBIR or other research;
   b. Value of SBIR project, including lay description of key technology objectives, current competition, and advantages to competing products or services, and any funding commitments from private sector or non-SBIR funding sources;
   c. Commercialization plans, milestones, target dates, market analyses of market size, and estimated market share after first year sales and after five years. The plan should state the amount and approximate dates that Phase III funds will be made available; and
   d. Patent status or other protection of project intellectual property.

Letters of Commitment. Offerors are encouraged to seek letters of interest or commitment(s) of funds and/or resources from an investor or partner organization for commercialization of the product(s) or service(s) resulting from the SBIR contract.

Fast-Track proposals that do not containing all parts described above will be redirected for Phase I consideration only.

The Phase I and Phase II proposals will be scored individually, and the scores for both phases will be totaled. Following the initial peer review, Fast-Track proposals may receive secondary review by the program staff of the respective NIH awarding component.

Fast-Track Phase II proposals may be funded following submission of the Phase I final report, and a determination that the Phase I objectives were met, feasibility was demonstrated, and funds are available.

VI. FAST-TRACK PHASE II PROPOSAL PREPARATION INSTRUCTIONS AND REQUIREMENTS

A. LIMITATIONS ON LENGTH OF PROPOSAL

SBIR Phase II proposals generally should not exceed a total of 150 single-spaced pages, including all enclosures and attachments. Pages should be of standard size (8 1/2" x 11") and the font should be no smaller than 10 point. Excluded from the page limitation are cover letters and letters from collaborators and consultants.

B. TECHNICAL PROPOSAL FORMAT AND CONTENT REQUIREMENTS

1. **Phase II Technical Proposal Cover Sheet**- Use Appendix D.
2. **Table of Contents**
3. **Abstract of the Research Plan**- Use Appendix B. State the broad, long-term objectives and specific aims. Do not include any proprietary information. Briefly and concisely describe the research design and methods for achieving these goals.
4. **Anticipated Results of Phase I Effort** - briefly discuss and summarize the objectives of your Phase I effort, the research activities to be carried out, and the anticipated results.
5. **Research Plan**
   a. *Detailed Approach and Methodology*- provide an explicit detail description of the Phase II approach. This section should be the major portion of the proposal and must clearly show advancement in the project appropriate for Phase II. Indicate not only what is planned, but also how and where the work will be carried out. List all tasks in a logical sequence to precisely describe what is expected of the contractor in performance of the work. Tasks should contain detail to (1) establish parameters for the project; (2) keep the effort focused on meeting the objectives; (3) describe end products and deliverables; and (4) describe periodic/final reports required to monitor work progress under the contract.

   b. *Personnel*- list by name, title, department and organization, the extent of commitment to this Phase II effort, and detail each person's qualifications and role in the project. ***Provide curricula vitae for all key staff members,*** describing directly related education, experience, and relevant publications. Describe in detail any involvement of subcontractors or consultants, and ***provide curriculae vitae for all key subcontractor staff. Also, include letters of commitment with proposed consultants confirming the extent of involvement and hourly/daily rate.***

   c. *Resources*- list/describe all equipment, facilities and other resources available for this project, including the offeror's clinical, computer and office facilities/equipment at any other performance site that will be involved in this project. Briefly state their capacities, relative proximity and extent of availability to this effort. (***Any equipment specifically proposed as a cost to the contract must be justified in this section as well as detailed in the budget. Equipment and products purchased with Government funds shall be American-made, to the extent possible. Title to the equipment will vest in the Government.)***

   d. *Other considerations* - provide a brief narrative of any unique arrangements, safety procedures in place, animal welfare issues, human subjects, etc. Note: If the research plan includes the use of human subjects or animals, refer to paragraphs IV. I-P of this solicitation for further guidance.

   e. *Appendices*

      (1) **Work Statement** - develop a Statement of Work similar in format to the sample in Appendix E. Create this from your detailed approach and methodology. It will be incorporated into the final contract document.

(2) **Product Development Plan** - comply with requirements referred to in *Section V.3.*)

6. **Summary of Related Activities** -use Appendix F.
7. **Technical Proposal Cost Information -** use Appendix C. Delete the fringe benefit costs, indirect costs and fee. Prepare a separate Appendix C for each year of the contract and a summary of the entire project.
8. **Number of Copies** -submit an original and 9 copies.

C. BUSINESS PROPOSAL FORMAT AND CONTENT REQUIREMENTS

1. **Cover Page** - use NIH Form 2043, Proposal Summary and Data Record, Appendix G.
2. **Breakdown of Proposal Estimated Costs, Fee and Labor Hours** - use Appendix C. Explain the basis for all costs and submit documentation to support all proposed costs must be submitted. Prepare a separate Appendix C for each year of the contract and a summary of the entire project.
3. **Number of Copies** - submit an original and 4 copies.

VII. METHOD OF SELECTION AND EVALUATION CRITERIA

Proposals will be initially screened to determine their compliance with the administrative requirements of this Solicitation and their applicability to the research topic selected by the offeror. Using the technical evaluation factors described below in Section VII.B., a peer review panel will evaluate proposals passing the initial screening for technical merit and scientific acceptability, to determine the most promising approaches.

A. EVALUATION PROCESS

Contract proposals are subjected to peer review by panels of scientists selected for their competence in relevant scientific and technical fields. The peer review panel will be responsible for evaluating proposals for scientific and technical merit and for performing a concept review, if one was not accomplished previously. The peer review panel provides a rating, makes specific recommendations related to the scope, direction and/or conduct of the proposed research, and for those proposals recommended for award, may provide a commentary about the funding level, labor mix and duration of the proposed contract project. The Institute program staff of the awarding component will conduct a second level of review. Recommendations of the peer review panel and program staff are based on judgments about not only the technical merit of the proposed research but also its relevance and potential contributions to the mission and programs of the awarding component. A Phase I or Phase II contract may be awarded only if the corresponding proposal has been recommended as technically acceptable by the peer review panel. ***Funding for any/all acceptable proposals is not guaranteed.***

B. TECHNICAL EVALUATION CRITERIA

In considering the technical merit of each proposal, the following factors will be assessed:

FACTORS FOR PHASE I PROPOSALS	WEIGHT
1. The soundness and technical merit of the proposed approach and identification of clear measurable goals (milestones) to be achieved during Phase I. (*Preliminary data are not required for Phase I proposals*.)	40%
2. The qualifications of the proposed principal investigator, supporting staff, and consultants.	20%
3. The potential of the proposed research for technological innovation.	15%
4. The potential of the proposed research for commercial application.	15%
5. The adequacy and suitability of the facilities and research environment.	10%

FACTORS FOR PHASE II PROPOSALS	WEIGHT
1. The scientific/technical merit of the proposed research, including adequacy of the approach and methodology, and identification of clear, measurable goals to be achieved during Phase II.	30%
2. The potential of the proposed research for commercialization and the adequacy of the Product Development Plan.	30%
3. The qualifications of the proposed principal investigator, supporting staff and consultants.	25%
4. The adequacy and suitability of the facilities and research environment.	15%

C. PROPOSAL DEBRIEFING

Offerors will be notified when they are no longer being considered for award. Offerors are entitled to one debriefing, which can be requested within three days of the receipt of the notification.

D. AWARD DECISIONS

For proposals recommended for award, the awarding component considers the following:

1. Ratings resulting from the scientific/ technical evaluation process;
2. Areas of high program relevance;
3. Program balance (i.e., balance among areas of research); and
4. Availability of funds.

The agency is not under any obligation to fund any proposal or make any specific number of contract awards in a given research topic area. The agency may also elect to fund several or none of the proposals received within a given topic area. The SBIR contract projects do not require establishing a competitive range or requesting final proposal revisions before reaching source selection decisions.

VIII. CONSIDERATIONS

A. AWARDS

1. The award instrument will be a contract.
2. A profit or fixed fee may be included in the proposal and the fee will be negotiated. A profit or fee is considered any amount in excess of actual direct and indirect cost incurred in the conduct of a project.
3. Phase I awards will be firm fixed price contracts. Normally, Phase II awards will be cost-plus-fixed-fee contracts.
4. The average dollar value of Phase I contracts to be awarded will be approximately $100,000. Phase II contracts normally may not exceed $750,000—including direct costs, indirect costs, and negotiated fixed fee.

Approximate number of Phase I contract awards:

AWARDING COMPONENTS		NO. OF AWARDS
National Institutes of Health (NIH)	National Institute on Alcohol Abuse and Alcoholism (NIAAA)	4
	National Cancer Institute (NCI)	2
	National Institute of Child Health and Human Development (NICHD)	2
	National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)	1
	National Institute on Drug Abuse (NIDA)	16
	National Institute of Environmental Health Sciences (NIEHS)	8
	National Institute of Mental Health (NIMH)	12-15
	National Institute of Neurological Disorders and Stroke (NINDS)	1

AWARDING COMPONENTS		NO. OF AWARDS
Centers for Disease Control and Prevention (CDC)	National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP)	11
	National Center for Environmental Health (NCEH)	3
	National Center for HIV, STD, and TB Prevention (NCHSTP)	8
	National Center for Infectious Diseases (NCID)	2
	National Center for Injury Prevention and Control (NCIPC)	3

B. FINAL REPORT

Original plus 2 copies

A final report is required of all Phase I and Phase II contractors. It should include a detailed description of the project objectives, the activities that were carried out, and the results obtained. An original and two copies of this report must be submitted as directed by the Contracting Officer not later than the expiration date of the Phase I contract.

Each Phase II "Fast-Track" contractor must submit semi-annual progress reports. A final report is required no later than the expiration date of the Phase II contract. *All reports (original plus two copies) must be submitted to the Contracting Officer.*

C. PAYMENT

The Government may make payments, including invoice and contract financing payments, by electronic funds transfer (EFT). As a condition to any payment, the contractor is required to provide information required to make payment by EFT.

Payments on Phase I contracts may be made on a monthly advance basis. Invoices/financing requests submitted for costs incurred under Phase II cost reimbursement contracts will be on a monthly basis unless otherwise authorized by the contracting officer.

D. LIMITED RIGHTS INFORMATION AND DATA

Proprietary Information. Information contained in unsuccessful proposals will remain the property of the offeror. The Government, however, may retain copies of all proposals. Public release of information in any proposal will be subject to existing statutory and regulatory requirements.

The Department of Health and Human Services (HHS) recognizes that, in responding to this Solicitation, offerors may submit information that they do not want used or disclosed for any purpose other than for evaluation. Such data might include trade secrets, technical data, and business data (such as commercial information, financial information, and cost and pricing data). The use or disclosure of such information may be restricted if offerors identify it and the Freedom of Information Act (FOIA) does not require its release. For information to be protected, offerors must identify in the Notice of Proprietary Information (on the Proposal Cover Sheet) the page(s) on which such information appears. Any other Notice may be unacceptable to the Government and may constitute grounds for removing the proposal from further consideration without assuming any liability for inadvertent disclosure.

Unless disclosure is required by the FOIA, as determined by FOI officials of the HHS, data contained in those portions of a proposal that have been identified as containing restricted information, in accordance with the Notice of Proprietary Information, shall not be used or disclosed except for evaluation purposes.

The HHS may not be able to withhold data that has been requested pursuant to the FOIA, and the HHS FOI officials must make that determination. The Government is not liable for disclosure if the HHS has determined that disclosure is required by the FOIA.

If a contract is awarded to the offeror as a result of, or in connection with, the submission of a proposal, the Government shall have the right to use or disclose the data to the extent provided by law. Proposals not resulting in a contract remain subject to the FOIA.

Rights to Data Developed Under SBIR Funding Agreement. Rights to data, including software developed under the terms of any funding agreement resulting from a contract proposal submitted in response to this Solicitation, shall remain with the awardee. However, the Government shall have the limited right to use such data for internal Government purposes and shall not release such data outside the Government without permission of the awardee for a period of four years from completion of each phase of the project under which the data was generated.

Copyrights. The awardee may normally copyright and publish (consistent with appropriate national security considerations, if any) material developed with PHS support. The awarding component receives a royalty-free license for the Federal Government and requires that each publication contain an acknowledgement of agency support and disclaimer statement, as appropriate. An acknowledgement shall be to the effect that: "This publication was made possible by contract number _____ from (*PHS awarding component*)" or "The project described was supported by contract number _____ from (*PHS awarding component*)."

Patents. Small business concerns normally retain the principal worldwide patent rights to any invention developed with Government support. Under existing regulations, 37 CFR 401, the Government receives a royalty-free license for Federal Government use, reserves the right to require the patent-holder to license others in certain circumstances, and requires that anyone exclusively licensed to sell the invention in the United States must normally manufacture it substantially in the United States.

To the extent authorized by 35 U.S.C. 205, the Government will not make public any information disclosing a Government-supported invention for a four-year period to allow the awardee a reasonable time to file a patent application, nor will the Government release any information that is part of that application.

Information about additional requirements imposed by 37 CFR 401 should be obtained from local counsel or from:

Office of Policy for Extramural Research Administration,
Extramural Inventions and Technology Resources Branch,
National Institutes of Health (NIH)
6701 Rockledge Drive
One Rockledge Building, Room 1136, MSC 7980,
Bethesda, MD 20892-7980
phone: (301) 435-1986 fax: (301) 480-0272
e-mail: gs60a@nih.gov

Inventions must be reported promptly—within two months of the inventor's initial report to the contractor organization—to the Division of Extramural Inventions and Technology Resources, NIH, at the address above. This should be done prior to any publication or presentation of the invention at an open meeting, since failure to report at the appropriate time is a violation of 35 USC 202, and may result in loss of the rights of the small business concern, inventor, and Federal Government in the invention. All foreign patent rights are immediately lost upon publication or other public disclosure unless a United States patent application is already on file. In addition, statutes preclude obtaining valid United States patent protection after one year from the date of a publication that discloses the invention.

The reporting of inventions can be accomplished by submitting paper documentation, including fax, or electronically through the NIH Edison Invention Reporting System. Use of the Edison system satisfies all mandated invention reporting requirements and access to the system is through a secure interactive Web site http://www.iedison.gov to ensure that all information submitted is protected. In addition to fulfilling reporting requirements, Edison notifies the user of future time sensitive deadlines with enough lead-time to avoid the possibility of loss of patent rights due to administrative oversight. Edison can accommodate the invention reporting need of all organizations. For additional information about this invention reporting and tracking system, visit the Edison home page cited above or contact Edison via e-mail at Edison@od.nih.gov.

Sharing Biomedical Research Resources. It is the policy of the NIH that unique research resources developed with NIH funding must be

shared with the research community. Restricted availability of these resources can impede the advancement of research. Principles and Guidelines for Recipients of NIH Research Grants and Contracts, as published in the Federal Register Notice on December 23, 1999 [http://ott.od.nih.gov/NewPages/RTguide_final.html], provide assistance to determine reasonable terms and conditions for acquiring and disseminating research tools, consistent with the objectives of furthering biomedical research and adhering to the Bayh-Dole Act.

Royalties. If royalties exceed $1,500, you must provide the following information on a separate page for each separate royalty or license fee:

1. Name and address of licensor.
2. Date of license agreement.
3. Patent numbers.
4. Patent application serial numbers, or other basis on which the royalty is payable.
5. Brief description (including any part or model number of each contract item or component on which the royalty is payable.)
6. Percentage or dollar rate of royalty per unit.
7. Unit price of contract item.
8. Number of units.
9. Total dollar amount of royalties.
10. If specifically requested by the Contracting Officer, a copy of the current license agreement and identification of applicable claims of specific patents (see FAR 27.204 and 31.205-37.)

E. PERFORMANCE OF RESEARCH AND ANALYTICAL WORK

In Phase I projects, normally a minimum of two-thirds or 67% of the research or analytical effort must be performed by the small business concern.

In Phase II projects, normally a minimum of one-half or 50% of the research or analytical effort must be performed by the small business concern.

The Contracting Officer must approve deviations from these requirements in writing.

Contractor Commitments. Upon entering into a contract, the contractor agrees, in accordance with the terms and conditions of the contract, to accept certain legal commitments embodied in the clauses of Phase I and Phase II contracts. The following list illustrates the types of clauses to which a contractor is bound. This list is not exhaustive. Copies of complete terms and conditions are available upon request.

Clauses That Apply to Contracts *NOT* Exceeding $100,000

1. ***Standards of Work.*** Work performed under the contract must conform to high professional standards.
2. ***Inspection.*** Work performed under the contract is subject to Government inspection and evaluation at all times.
3. ***Termination for Convenience.*** The Government may terminate the contract at any time for convenience if it deems termination to be in its best interest, in which case the contractor will be compensated for work performed and for reasonable termination costs.
4. ***Disputes.*** Any dispute concerning the contract that cannot be resolved by agreement shall be decided by the contracting officer with right of appeal.
5. ***Equal Opportunity.*** The contractor will not discriminate against any employee or applicant for employment because of race, color, religion, sex, or national origin.
6. ***Affirmative Action for Veterans.*** The contractor will not discriminate against any employee or applicant for employment because he or she is a disabled veteran or veteran of the Vietnam era.
7. ***Affirmative Action for Handicapped.*** The contractor will not discriminate against any employee or applicant for employment because he or she is physically or mentally handicapped.
8. ***Gratuities.*** The Government may terminate the contract if any gratuities have been offered to any representative of the Government to secure the contract.
9. ***American-made Equipment and Products.*** When purchasing equipment or products under an SBIR contract award,

the contractor shall purchase only American-made items whenever possible.

Clauses That Apply to Contracts Exceeding $100,000

In addition to the foregoing clauses, the following clauses apply to contracts expected to exceed $100,000.

10. ***Examination of Records.*** The Comptroller General (or a duly authorized representative) shall have the right to examine any directly pertinent records of the contractor involving transactions related to this contract.
11. ***Default.*** The Government may terminate the contract for default if the contractor fails to perform the work described in the contract and such failure is not the result of excusable delays.
12. ***Contract Work Hours.*** The contractor may not require an employee to work more than eight hours a day or forty hours a week unless the employee is compensated accordingly (i.e., overtime pay).
13. ***Covenant Against Contingent Fees.*** No person or agency has been employed to solicit or secure the contract upon an understanding for compensation except bona fide employees or commercial agencies maintained by the contractor for the purpose of securing business.
14. ***Patent Infringement.*** The contractor shall report each notice or claim of patent infringement based on the performance of the contract.

F. ADDITIONAL INFORMATION

1. This Solicitation is intended for informational purposes and reflects current planning. If there is any inconsistency between the information contained herein and the terms of any resulting SBIR contract, the terms of the contract are controlling.
2. Prior to award of an SBIR contract, the Government may request the offeror to submit certain organizational, management, personnel and financial information to assure responsibility of the offeror to receive an award.
3. The Government is not responsible for any expenditures of the offeror in advance and in anticipation of an award. In a cost reimbursement contract, reimbursement of costs by the Government may be made only on the basis of costs incurred by the contractor after award and during performance.
4. This Solicitation is not an offer by the Government and does not obligate the Government to make any specific number of awards. Awards under this program are contingent upon the scientific/technical merit of proposals and the availability of funds.
5. The SBIR program is not intended as a mechanism to invite unsolicited proposals. Unsolicited proposals shall not be accepted under the SBIR program in either Phase I or Phase II.
6. If an award is made pursuant to a proposal submitted in response to this SBIR Solicitation, the contractor will be required to certify that he or she has not previously been, nor is currently being, paid for essentially equivalent work by any agency of the Federal Government.
7. Prior to award of a contract, the contractor will be required to provide a Data Universal Numbering System (DUNS) number. A DUNS number may be obtained immediately, at no charge, by calling Dun and Bradstreet on (800) 333-0505.

IX. INSTRUCTIONS FOR PROPOSAL SUBMISSION

A. RECEIPT DATE

The deadline for receipt of all contract proposals submitted in response to this Solicitation is:
5:00 p.m., Eastern Standard Time
Friday, November 9, 2001

Any proposal received at the offices designated below after the exact time specified for receipt will not be considered unless it is received before award is made and:

1. It was sent by registered or certified mail not later than the fifth calendar day prior to the date specified for receipt of proposals;

2. It was sent by mail or hand-delivered and it is determined by the Government that the late receipt was due primarily to mishandling by the Government after receipt at the Government installation;

3. It was transmitted through an electronic commerce method authorized by the Solicitation and was received at the initial point of entry to the Government infrastructure not later than 5:00 p.m. one working day prior to the date specified for receipt of proposals;

4. It is the only proposal received, or;

5. It is received in the office designated for receipt of proposals on the first workday on which normal Government processes are resumed following an emergency or anticipated event that interrupts normal Government processes so that proposals cannot be received by the exact time specified in the Solicitation.

Despite the specified receipt date above, a proposal received after that date may be considered if it offers significant costs or technical advantages to the Government and it was received before proposals were distributed for evaluation, or within 5 calendar days after the exact time specified for receipt, whichever is earlier.

B. NUMBER OF COPIES

For Phase I, submit the original and 5 copies of each proposal. The principal investigator and a corporate official authorized to bind the offeror must sign the original. The 5 copies of the proposal may be photocopies of the original.

For Phase II, see instructions under paragraph VI.

C. BINDING AND PACKAGING OF PROPOSAL

Send all copies of a proposal in the same package. Do not use special bindings or covers. Staple the pages in the upper left corner of each proposal.

X. CONTRACTING OFFICERS AND ADDRESSES FOR MAILING OR DELIVERY OF PROPOSALS

Any small business concern that intends to submit an SBIR contract proposal under this Solicitation should provide the appropriate contracting officer(s) with early, written notice of its intent, giving its name, address, telephone, and topic number(s). If a topic is modified or canceled before this Solicitation closes, only those companies that have expressed such intent will be notified.

A. NATIONAL INSTITUTES OF HEALTH (NIH)

National Institute on Alcohol Abuse and Alcoholism (NIAAA)

Ms. Roberta Wilhelm
Phone: (301) 443-1191
Fax: (301) 443-3891
E-mail: rwilhelm@willco.niaaa.nih.gov

Proposals to the NIAAA must be mailed or delivered to:

Ms. Roberta Wilhelm
Contracting Officer
Contracts Management Branch
National Institute on Alcohol Abuse and Alcoholism
6000 Executive Blvd., Suite 504
Bethesda, MD 20892-7003 *

**Change the city to Rockville and the zip code to 20852 if hand-delivered or delivered by an overnight service to the NIAAA.*

National Cancer Institute (NCI)

Mr. Joseph Bowe
Phone: (301) 435-3810
Fax: (301) 480-0309
E-mail: jb166i@nih.gov

Proposals to the NCI, *if mailed through the U.S. Postal Service*, must be addressed as follows:

Mr. Joseph Bowe
Contracting Officer
Research Contracts Branch,
National Cancer Institute
6120 Executive Blvd., EPS Room 608
Bethesda, MD 20892-7222 *

*Change the city to Rockville and the zip code to 20852 if hand-delivered or delivered by an overnight service to the NCI.

National Institute of Child Health and Human Development (NICHD)

Ms. Mya Hlaing
Contracting Officer
Phone: (301) 496-4611
Fax: (301) 402-3676
E-mail: mh89m@nih.gov

Proposals to the NICHD must be mailed or delivered to:

Contracts Management Branch, OAM
National Institute of Child Health & Human Development, NIH
6100 Executive Boulevard, Suite 7A07
Bethesda, MD 20892-7510 *

**Change the city to Rockville and the zip code to 20852 if hand-delivered or delivered by an overnight service to the NICHD.*

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

Mr. Patrick Sullivan
Phone: (301) 594-7728
Fax: (301) 480-4226
E-mail: ps55w@nih.gov

Proposals to the NIDDK must be mailed or delivered to:

Mr. Patrick Sullivan
Chief, Acquisition Management Branch
National Institute of Diabetes and Digestive and Kidney Diseases
6707 Democracy Blvd.
Room 781, MSC 5453
Bethesda, MD 20892-5453 *

**Change the city to Rockville and the zip code to 20817 if hand-delivered or delivered by an overnight service to the NIDDK.*

National Institute on Drug Abuse (NIDA)

Ms. Nikki Zangwill
Phone: (301) 443-6677
Fax: (301) 443-7595
E-mail: nz2f@nih.gov

Proposals to the NIDA must be mailed or delivered to:

Ms. Nikki Zangwill
Contracting Officer, Contracts Management Branch
National Institute on Drug Abuse
6001 Executive Boulevard
Room 3105, MSC 9543
Bethesda, Maryland 20892-9543 *

**Change the city to Rockville and the zip code to 20852 if hand-delivered or delivered by an overnight service to the NIDA.*

National Institute of Environmental Health Sciences (NIEHS)

Mr. Phillip D. Jones
Phone: (919) 541-0426
Fax: (919) 541-2712
E-mail: pj13c@nih.gov

Proposals to the NIEHS must be mailed or delivered to:

Mr. Phillip D. Jones
Contracting Officer
Contracts and Research Branch, DERT
National Institute of Environmental Health Sciences
P. O. Box 12874
Research Triangle Park, NC 27709

Proposals to the NIEHS, *if hand-delivered or delivered by an overnight service*, must be addressed as follows:

Mr. Phillip D. Jones
Contracting Officer
Contracts and Research Branch, DERT
National Institute of Environmental Health Sciences
79 T.W. Alexander Drive, Building 4401
Research Commons
Research Triangle Park, NC 27709

National Institute of Mental Health (NIMH)

Mr. David Eskenazi
Phone: (301) 443-2696
Fax: (301) 443-0501
E-mail: de5d@nih.gov

Proposals mailed to the NIMH must be addressed to:

Mr. David Eskenazi

Contracting Officer
Chief, Contracts Management Branch
National Institute of Mental Health
6001 Executive Boulevard
Room 6107, MSC 9603
Bethesda, Maryland 20892-9603 *

*Change the city to Rockville and the zip code to 20852 if hand-delivered or delivered by an overnight service to the NIMH.

National Institute of Neurological Disorders and Stroke (NINDS)

Mr. Kirkland L. Davis
Phone: (301) 496-1813
Fax: (301) 402-4225
E-mail: kd17c@nih.gov

Proposals mailed to the NINDS must be addressed to:

Mr. Kirkland L. Davis
Chief, Contracts Management Branch
National Institute of Neurological Disorders and Stroke, NIH
Neuroscience Center, Suite 3287
6001 Executive Boulevard, MSC 9531
Bethesda, Maryland 20892-9531 *

*Change the city to Rockville and the zip code to 20852 if hand-delivered or delivered by an overnight service to the NINDS.

B. CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)

National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP)

National Center for Environmental Health (NCEH)

National Center for HIV, STD, and TB Prevention (NCHSTP)

National Center for Infectious Diseases (NCID)

National Center for Injury Prevention and Control (NCIPC)

Ms. Jamie Legier
Phone: (770) 488-2635
Fax: (770) 488-2670
Email: JLegier@cdc.gov

Proposals to the NCCDPHP, NCEH, NCHSTP, NCID and the NCIPC must be mailed or delivered to:

Ms. Jamie W Legier
Contracting Officer, Department of Health and Human Services
Centers for Disease Control and Prevention
Procurement and Grants Office
2920 Brandywine Rd, Rm 3123
Atlanta, GA 30341

XI. SCIENTIFIC AND TECHNICAL INFORMATION SOURCES

Health science research literature is available at academic and health science libraries throughout the United States. Information retrieval services are available at these libraries and Regional Medical Libraries through a network supported by the National Library of Medicine. A list of Regional Medical Libraries and information about network services may be requested from the Public Information Office, National Library of Medicine, Bethesda, MD 20894, (301) 496-6308.

Other sources that provide technology search and/or document services include the organizations listed below. They should be contacted directly for service and cost information.

National Technical Information Service

5285 Port Royal Road
Springfield, VA 22161
(703) 487-4600

Mid-Atlantic Technology Applications Center

University of Pittsburgh
823 William Pitt Union
Pittsburgh, PA 15260
(412) 648-7000
(412) 648-7003 (Fax)
(800) 257-2725 (toll-free US)

Mid-Continent Technology Transfer Center

The Texas A&M University System
College Station, TX 77843-3401
(409) 845-8762

(409) 845-3559 (Fax)

Great Lakes Industrial Technology Center

25000 Great Northern Corporate Center
Suite 260
Cleveland, OH 44070-5310
(216) 734-0094

Center for Technology Commercialization

Massachusetts Technology Park
100 North Drive
Westborough, MA 01581
(508) 870-0042

Southern Technology Applications Center

University of Florida
College of Engineering
Box 24
One Progress Boulevard
Alachua, FL 32615
(904) 462-3913
(800) 225-0308 (outside FL)

Far West Regional Technology Transfer Center

University of Southern California
3716 South Hope Street, Suite 200
Los Angeles, CA 90007-4344
(213) 743-6132
(213) 746-9043 (Fax)
(800) 642-2872 (CA only)
(800) 872-7477 (outside CA)

National Technology Transfer Center

Wheeling Jesuit College
316 Washington Avenue
Wheeling, WV 26003-6295
(800) 678-6882 (toll-free US)

(All services at no cost)

XII. RESEARCH TOPICS

NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM (NIAAA)

The NIAAA supports research on the causes, prevention, control, and treatment of the major health problems of alcohol abuse, alcoholism, and alcohol-related problems. Through its extramural research programs, the NIAAA funds a wide range of basic and applied research to develop new and/or improved technologies and approaches for increasing the effectiveness of diagnosis, treatment, and prevention. The NIAAA also is concerned with strengthening research dissemination, scientific communications, public education, and data collection activities in the areas of its research programs.

This Solicitation invites proposals in the following areas:

017 Development of Methodology for Measuring Compliance for Medications

Currently, NIAAA is funding over 20 human pharmacotherapy studies. It appears that the efficacy of medications is dependent, in part, on patient compliance. Measurement of patient compliance in pharmacotherapy trials and medical practice, however, is difficult. Current methods employed include pill counts, electronic pillboxes, riboflavin, and plasma levels of the medication. The purpose of this contract is to develop innovative methods for measuring patient compliance in administering medications. Women and minorities should be included in the study.

Phase I should entail development and early, pre-clinical testing of the technique for measuring compliance. Phase II would involve larger-scale evaluations to determine the validity of the technique. This would involve measuring compliance using a double-blind, placebo-controlled pharmacologic trial.

018 Medications Development

Over the past decade, research on possible pharmacologic agents for treatment of excessive alcohol consumption has burgeoned. Drinking

behavior is complex and appears to involve numerous neurotransmitter systems, including the opioid, serotonin, dopamine, GABA, and glutamate systems. Various medications interact with these neurotransmitter systems. In order to obtain FDA approval, preclinical development with animal models and clinical development with humans must be conducted under FDA specifications. This contract is seeking applications to help develop medications for the treatment of excessive alcohol consumption that appear promising on the basis of the existing scientific literature. Women and minorities should be included in the study.

Phase I of the requested SBIR contract should involve the development and early-phase preclinical and/or clinical testing of a specified medication for efficacy, toxicity, pharmacokinetics, formulation, and stability under Good Manufacturing Practice (GMP) or Good Laboratory Practice (GLP) conditions. Phase II would involve larger-scale and more definitive studies to determine the efficacy, toxicology, pharmacokinetics, formulation, or stability under GMP or GLP conditions. Animal models and/or humans should be used. Positive findings from these studies may also be purchased by a pharmaceutical firm for further drug development.

022 Science Education Materials Development for Middle Schools or High Schools

Approximately one million youth, ages 12-17, are consuming alcohol. Experimentation with alcohol is beginning at ever-younger ages. Moreover, research suggests that the earlier the onset of drinking, the more likely it is that an individual will develop drinking-related problems in adulthood. Nearly 14 million American adults develop problems from drinking. Specific problems include health deterioration (including death) from damage to the brain, liver, gastrointestinal tract, and/or heart; injuries such as automobile crashes and household/workplace accidents; domestic and other forms of violence; neglect of work and family, and costs to society associated with police, courts, jails, and unemployment. Problems of adolescent drinking include poor school performance, absenteeism and dropping out; use/abuse of other drugs; psychological and social maladjustment; and criminal involvement. Nevertheless, alcohol use is part of the American culture, and most adults who drink do so with a minimum of risk. Thus, despite what young people are taught in health education or physical education about the potential for alcohol use to cause them problems, many take drinking for granted--regarding it as a common "rite of passage" to adulthood, especially for boys.

Purpose. Few curricular materials about substance abuse generally, and alcohol abuse specifically, are science-based. Rather, they focus on substance abuse awareness and on social influence--the importance of personal self-esteem, and on building refusal skills. This health education approach is indeed valuable, but it is not enough. For example, being told in a health education class that alcohol use by underage drinkers can cause cognitive damage is very different from learning the *science*, or the *why* behind this finding. Moreover, "telling" is not always "teaching". The critical thinking skills involved in the methodology of doing science are learned in science education, not in health education. Critical thinking is an invaluable asset in personal decision-making.

The purpose of the NIAAA science education program is to support the infusion of research findings into supplementary, interdisciplinary, curriculum materials and educational technology-based activities that help make the represented disciplines (science, math, social studies, English composition, and/or more) relevant to an issue in the student's life. Specifically, the NIAAA science education program is designed to support middle-school and high school teachers help students to enjoy the process of discovery in accordance with the National Science Education Standards (1996), and to appreciate how medical science generally, and alcohol science specifically, addresses public health issues.

Objectives and Curricular Needs. The overall objective is to reinforce and complement the social influence model of substance abuse prevention with scientific knowledge to support student decision-making processes and skills. Because fact-based information on alcohol and how it affects the human body (and other living organisms) is available and objective, it should be readily teachable and integratable into existing school curricula.

The supplementary curriculum materials developed should be both scientifically valid and age- or grade-appropriate. Project design should address performance objectives in relation to the chosen grade level(s) and subject(s)/discipline(s).

The materials developed should include both background information and instructional guidance for teachers, recognizing that many teachers, especially at the middle-school level, may lack sufficient education in science, mathematics, or technology themselves, and may be uncomfortable and unprepared to teach science concepts, statistical methods, and related disciplines. The materials should be "teacher-friendly" while promoting active, teacher-guided, student-conducted scientific inquiry. Project design should address instructional objectives.

Discovery-based activities centered around case studies to guide classroom discussion; active engagement in laboratory work; cooperative learning activities in small groups with access to resource materials and with group presentation of findings/information are all encouraged. Resulting materials should utilize/reflect educational technologies as appropriate--while ensuring that a core curriculum and associated materials are print-based for the benefit of under-resourced schools. Similarly, hands-on laboratory activities should require only commonly available supplies. Streaming video, computer simulations, and other venues for conveying more complex laboratory activities may be included--if transferable to other media for under-resourced schools, e.g. videotape in lieu of streaming video. Project design should address the selection of instructional technologies/media.

Evaluation components--whether embedded or separate--to assess student learning, age-appropriate relevance, and teacher satisfactions or instructional difficulties (such as which activities work well and which do not) shall be included. Evidence of plans to ensure focus group(s), a scientific advisory board, and/or field testing, as appropriate, should be included in the project design.

023 Search of Human Heart Genes Differentially Expressed Following Moderate Alcohol Consumption/Exposure

Moderate alcohol consumption is associated with reduced risk of coronary artery disease (CAD). Whether this effect is mediated by the direct action of alcohol on the heart is controversial. The purpose of this project is to determine if moderate alcohol exposure mediates changes in gene expression in the human myocardium and coronary vasculature. This proposal will study the effects of alcohol on nonischemic, "normal" human myocardium, obtained from pediatric, congenitally malformed hearts. These hearts generally represent a source of "disease free" vasculature which will be essential to ensure proper perfusion and infusion of alcohol to the hearts. Ordinarily, these hearts are discarded as surgical waste after completion of the transplant. Alternatively, explanted hearts from selective patients undergoing transplantation will be used. An alcohol response will be simulated by perfusing the **explanted/discarded** hearts without/with moderate alcohol (<0.1%) in different regions (vascular beds) of the same heart. Gene expression profiles of tissues from the ventricle and the coronary arteries will be examined using DNA microchip arrays. Comparison of the expression profiles in the exposed and unexposed tissues should reveal if moderate levels of alcohol directly alter the pattern of gene expression in the human heart and vasculature. These analyses will identify highly responsive genes, reveal if specific metabolic pathways or groups of genes that are coordinately affected, and identify new alcohol responsive genes. Thus, the project should provide an invaluable new resource for the NIH/NIAAA and other alcohol researchers for further analyses of alcohol-mediated alterations in gene expression. The availability of this resource would greatly facilitate studies on alcohol-induced effects on the cardiovascular system including cardioprotection, CAD, cardiomyopathy, arrhythmias, hypertension and stroke.

Human Hearts. Explanted hearts from pediatric patients with congenital heart disease undergoing cardiac transplantation would provide a source of "nonischemic or myopathic" myocardium with normal, nonatherogenic coronary arteries. Explanted hearts with ischemic damage or severe ventricular dilatation will be excluded. Alternatively, hearts from patients with primary pulmonary hypertension

undergoing heart/lung transplantation may be used in light of their normal left ventricular size and function. These hearts are less desirable because the likelihood of undetected CAD is higher than that in the pediatric population. Two to three hearts will be used over the contract period.

The explanted human hearts will be perfused using a modified Langendorff procedure (3) which is a highly versatile perfusion system consisting of a temperature-controlled reservoir, a peristaltic pump, electronic controller, an inline transducer to continuously monitor pressure and a temperature-controlled organ chamber. Initially, two main coronary arteries representing different vascular territories will be perfused simultaneously with the same perfusate. Subsequently, one of these coronary arteries will be switched to a perfusate containing 0.1% alcohol for 60 minutes utilizing a separate pump. The perfusate will be discarded after one pass through the heart. The hearts will then be maintained for an additional 2 hours. This length of time should not present a problem for myocardial viability as Langendorff perfused hearts can generally be kept functional for up to 3-4 hours as long as continuous perfusion is maintained. Upon completion of the protocol, transmural specimens of the myocardium near the coronaries and sections of the coronary arteries themselves will be collected and frozen in liquid nitrogen. Potential differences in the genetic response of the right and left ventricular myocardium to alcohol will be analyzed using selective engagement of the left anterior descending, circumflex and right coronary arteries.

Gene Expression Profiling. An Affymetrix system for probing and analyzing oligonucleotide array will be used. The system will allow us to probe approximately 7,000 known human genes and 35,000 expressed sequence tags. To survey expression profiles, RNA will be isolated from the frozen tissues by standard procedures, and biotinylated cRNA probes prepared. The proposed analyses will be carried out in duplicate and would require at least 8 sets of the human gene arrays. The quality of the probes will be verified by hybridization to "test" chips and then used to probe the full array. Scanning of the chip and "scaling" of the hybridization signals is carried out by the system. By equalizing the scaling, as well as assessing expression of a number of controls on the chips, results obtained with different sample probes can be compared. Thus, the data files could also be compared to gene expression profiles obtained in other laboratories.

Evaluating the biologic significance of changes in gene expression will still require substantial analysis. The sensitivity of the current technology is a 2-fold change in expression. Since alcohol induces more than a 2-fold change in the expression of tissue plasminogen activator, urokinase and PAI-1 genes in cultured endothelial cells (4,5), the effects of moderate alcohol on the intact heart will be assessed by monitoring the expression of these genes in the vascular tissue. The levels of change detected for these genes will be used as criteria to identify other changes in gene expression that may have physiologic relevance. This analysis will indicate whether moderate alcohol exposure induces changes in gene expression in the myocardium. The change in the pattern of gene expression in muscle vs. vascular tissues would serve to distinguish responses that are unique to particular tissue from those that may be common to all cells. Moreover, because of the global nature of the analysis, it is likely that new and unanticipated genes or pathways affected by alcohol will be detected. Thus, this analysis of gene expression would help to identify new potential molecular mediators of the alcohol response. Such information would be extremely useful in further defining the molecular mechanisms that may underlie and contribute to cardioprotection.

One caveat is that the information is limited to the genes that are included in the arrays, may not detect low abundance gene with modest changes in gene expression, and may also be limited to genes that change their expression within the 3-hour time frame of the experiment. More extensive arrays are likely in the future and will be used to extend the survey. Regional responses of the ventricle to alcohol would also be assessed.

Phase I: Set up the perfusion system and ensure that the protocols for generating the molecular probes and for gene profiling are operational. By the end of the phase I, it is anticipated that the analysis on at least one explanted human heart is carried out.

Phase II: In the second year, the results of the initial survey will be verified by examining another explanted heart. The effect of altering

the exposure to alcohol or signal variation in gene expression may also be addressed depending on the results in phase I. A database of the affected genes will be available for the alcohol research community.

Literature Cited. (1) Gordon T, Kannel WB: Drinking habits and CVD: The Framingham Study. Am Heart J 105:667-673, 1993.

(2) Doll R: One for the Heart. Br Med J 315:1664-1668, 1997.

(3) Walters HL, Digerness SB, Naftel DC, Waggoner JR, Blackstone EH, Kirklin JW: The response to ischemia in blood perfused vs. crystalloid perfused isolated rat heart preparations. J Mol Cell Cardiol 24: 1063-1077, 1992.

(4) Grenett HE, Torres JA, Demissie S, Tabengwa EM, Davis GC, Booyse FM: Ethanol transcriptionally upregulates t-PA and u-PA gene expression in cultured HUVECs. Alcohol Clin Exp Res 22:849-853, 1998.

(5) Grenett HE, Aikens ML, Tabengwa EM, Davis GC, Booyse FM: Ethanol downregulates transcription of the PAI-1 gene in cultured HUVECs. Thrombosis Research, in press.

NATIONAL CANCER INSTITUTE (NCI)

The NCI is the Federal Government's principal agency established to conduct and support cancer research, training, health information dissemination, and other related programs. As the effector of the National Cancer Program, the NCI supports a comprehensive approach to the problems of cancer through intensive investigation in the cause, diagnosis, prevention, early detection, treatment, rehabilitation from cancer, and the continuing care of cancer patients and families of cancer patients. To speed the translation of research results into widespread applications, the National Cancer Act of 1971 authorized a cancer control program to demonstrate and communicate to both the medical community and the general public the latest advances in cancer prevention and management.

This Solicitation invites proposals in the following area:

181 Clinical Trials Data Collection Using Hand Held Technology

The Cancer Treatment Evaluation Program, CTEP, has been advancing recommendations for the streamlining of cancer clinical trials. Several of the pilot projects have demonstrated areas where efficiencies can be achieved. One such area is the data collection of clinical trials data. Over the past several years, CTEP has developed several data standards and streamlined approaches, including Common Data Elements for trials, the Common Toxicity Criteria, and the Cancer Trials Support Unit. Industry and others have adopted much of this work. CTEP proposes this SBIR topic to exploit these other products and projects.

The current paradigm is to use paper reports, send them to operations offices, or carry the paper to networked computers, and enter the data. When errors are found, the paper case report form is taken back to medical records areas, corrected, and the data is then once again entered. CTEP is requesting SBIR proposals, which will develop integrated and automated applications to overcome the entropy of this current paradigm.

Handheld equipment have been integrated in similar data collection environments, and the technology is advancing at an exponential rate. It no longer makes sense to ignore the ability to enter information once, have it checked for some accuracy, and reuse it throughout the life of a clinical trial.

The successful offeror shall fully utilize the CDE (Common Data Elements), CTC (Common Toxicity Criteria), and CTSU data requirements and standards, and provide research collaborators with tools to minimize the effort required to correctly enter case report data. The system developed shall also integrate with the commercial Oracle Clinical product, the repository system for the CTSU. The system developed shall, with minimal effort, replicate any case report form, using the information stored in the CTSU, CDE, and CTC repositories.

CTEP will identify and coordinate users to be included in beta testing, and the knowledge acquisition, KA, phase of this effort. CTEP will provide ongoing guidance and monitor compliance with the stated standards.

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT (NICHD)

The NICHD conducts and supports research and research training on biological and behavioral aspects of human development. Primary program areas include: reproduction and population studies, pregnancy, perinatal biology, maternal and infant well-being, developmental and reproductive immunology, congenital defects, developmental biology, nutrition and growth, child development and behavior, human learning and learning disabilities, cognitive and social development, mental retardation and developmental disabilities, AIDS and HIV, and medical rehabilitation. For additional information about areas of interest to the NICHD, please visit our home page at http://www.nichd.nih.gov/.

This Solicitation invites proposals in the following area:

021 Skeletal Fixation of Prosthetic Limbs *(accepting Fast Track proposals)*

The National Center for Medical Rehabilitation Research (NCMRR) of the NICHD is seeking potential contractors with an interest in developing improved biomaterials and animal models to demonstrate the potential for direct skeletal attachment of prosthetics. Some of the techniques associated with successes relating to dental implants and joint replacements may be translated to transcutaneous prosthetic limbs. Limited skeletal attachment studies to date on amputees in England and Sweden have made initial progress. However, the required connection of the implant with both hard and soft tissues of the residual limb leaves distinct tissue implant interfacial problems associated with 1) either fixation in bone, or 2) soft tissue attachment in the transcutaneous region. Therefore, to make direct skeletal attachment of prosthetics (implantation) both comfortable and practical, it is necessary to improve biomaterials and test this material in animal studies. Thus, the NCMRR solicits applications for projects devoted to the following:

1. Development of materials that increase bone biomaterial interfacial bond strength and accelerate bone formation surrounding implants.
2. Development of animal studies that increase both initial and long-term implant stability, prevent epithelial cell invasion, and promote functional adaptation of both soft and hard tissues.

NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES (NIDDK)

The NIDDK supports research in diabetes, endocrinology and metabolic diseases; digestive diseases and nutrition; and kidney, urologic, and hematologic diseases.

This Solicitation invites proposals in the following area:

074 Noninvasive Measurement of Body Iron in Humans

Objective: There is a pressing need to be able to perform non-invasive measurements of body iron stores. The need has been recognized for a long time in thalassemia patients who receive chronic blood transfusions. More recently, sickle cell patients at risk for stroke have been transfused more regularly, and there has been consideration of iron measurements in individuals with hemochromatosis mutations. Serial measurements of plasma ferritin have had some utility, but are highly variable from one individual to the next. For many years, thalassemia patients have had their liver iron stores assessed using a SQUID (superconducting quantum interference device), which has been shown to correlate well with biopsy results. However, the present SQUID is expensive, is located in very few sites, and is not suited for some situations, such as heart measurements. The most prominently mentioned alternative is magnetic resonance imaging (MRI). MRI equipment is widely available, but there are questions of standardization of measurements among various facilities. MRI measurements depend upon the complex interactions of several iron-binding proteins and water protons that are incompletely understood. Also, MRI sensitivity appears to be decreased at higher level of iron, limiting its utility in heavily loaded individuals. Several other methods have been proposed, with less likelihood of clinical utility, including nuclear resonance scattering of X-rays and computed tomography (CT).

Description: Small Business Innovation Research (SBIR) contract proposals are solicited based on recommendations received in the course of the recent NIDDK Workshop on Noninvasive Measurement of Iron, April 17,

2001.
(http://www.niddk.nih.gov/fund/other/conferences.htm#3)

1. MRI. Currently, it is not practical to directly measure iron by MRI. Therefore, iron must be detected by the indirect effect it has on MR relaxation time (or possibly susceptibility shifts). The successful detection of iron overload requires three basic things: (1) appropriate MR measurement method(s), (2) optimized RF coils for the body region of interest, and (3) magnets of the appropriate magnetic field strength(s).

    - A reliable method needs to be developed for calibrating and validating iron concentration detected by magnetic resonance imaging.

    - The most appropriate magnetic resonance method for determining relaxation times and susceptibility needs to be investigated. What data acquisition method is best with what timing parameters? Should a mono-exponential or bi-exponential model be used to guide data collection and to fit the relaxation data? What is the best method of selecting a region-of-interest? What is an acceptable level of signal-to-noise?

    - The mechanistic contribution of iron in iron-containing materials (e.g. ferritin and hemosiderin) to magnetic resonance relaxation needs to be understood so that detailed predictions can be used to guide future developments. This information will provide guidance in the selection of the optimum measurement field strength and methods.

    - The structure of iron in ferritin and hemosiderin, and the biological distribution of these macromolecular assemblies, need to be understood more fully.

    - A careful comparison between methods of iron detection needs to be performed [i.e. magnetic resonance imaging and susceptometry

    - Explore the development of indicator materials for direct MR measurement of iron concentration.

2. SQUID. At present, biomagnetic susceptometry provides the only non-invasive method for measurement of tissue iron stores that has been calibrated, validated and used in clinical studies but the complexity, cost and technical demands of the liquid-helium-cooled superconducting instruments now required have restricted clinical access to the method.

    - Investigative initiatives are needed to develop innovative susceptometry techniques that are suitable for routine clinical use in studies of iron overload. Possible approaches include: Liquid-nitrogen cooled instrumentation exploiting the phenomenon of high-temperature superconductivity, devices using non-superconducting components such as magnetoresistive sensors, and magnetic resonance imaging instruments adapted for magnetic susceptibility measurement.

    - Additional research is needed to improve the accuracy and precision of biomagnetic susceptometry so as to make possible resolution of iron concentrations encountered in iron deficiency.

    - Basic research is needed to more precisely characterize the magnetic susceptibility of iron in ferritin and hemosiderin and the sources and extent of variations in the susceptibility of these compounds.

    - Research is required to explore the potential that exists for developing the rudimentary imaging capability of current susceptometry into the sort of susceptibility tomography that would allow measurement of tissue iron concentrations in the heart, pancreas, brain and other organs.

NATIONAL INSTITUTE ON DRUG ABUSE (NIDA)

NIDA's mission is to lead the nation in bringing the power of science to bear on drug abuse and addiction, through support and conduct of

research across a broad range of disciplines and by ensuring rapid and effective dissemination and use of research results to improve prevention, treatment, and policy.

This Solicitation invites proposals in the following areas:

010 Analytical Techniques Program
(accepting Fast Track proposals)

The purpose of this contract is to develop new analytical methods or reagents for use in measuring drugs of abuse and their metabolites in biological systems, such as urine, blood, saliva, sweat, hair, breast milk, brain tissue, and meconium. An additional example would be the determination of second hand smoke from volatile drugs of abuse. The modifications and improvements in existing analytical techniques would also be considered, particularly those improving sensitivity and selectivity.

Phase I proposal should be used to demonstrate the technical merit and feasibility of the project. Under phase II proposal the methods and /or equipment should be finalized, and its commercial potential demonstrated.

028 Prevention Training
(accepting Fast Track proposals)

Prevention research has established a significant wealth of information regarding effective substance abuse prevention programs. Previous PRB SBIR contracts have focused on prevention research dissemination (mechanisms which are utilized to transfer drug abuse prevention information to practitioners, policy makers, and the public) and measurement modules for prevention interventions (aiding various groups to identify existing or develop new measures of the antecedents, mediators and outcomes thought to be associated with the interventions). This solicitation seeks development of materials and methods for training trainers and prevention intervention delivery personnel in ways that ensure the program is implemented with fidelity.

The purpose of Phase I would be to identify effective ways to package substance abuse prevention training materials and to develop effective methods for training trainers and prevention delivery personnel. Key concepts of program delivery such as recruitment and retention and fidelity of implementation would be addressed. Development of innovative models and methods for training and implementation, such as the infusion model, are encouraged.

Phase II would involve implementation development and effectiveness testing of training materials and modules at the trainer and intervention delivery levels in real world settings. Plans for marketing of training at both levels would be presented.

029 Development of Science Education Materials or Programs
(accepting Fast Track proposals)

For many years, students in the United States have scored poorly on standardized tests relative to their international peers. Furthermore, student interest in science has been declining. At the same time, public science literacy has remained low. Low science literacy among students and other groups has many implications. In order for NIDA to fulfill its mission, there is a need to ensure that adequate numbers of students are entering science education tracks and eventually pursuing careers in biomedical sciences. It is also important to the mission of NIDA that other groups, such as the general public, health care workers, etc. are scientifically literate. It is particularly important to NIDA that all members of society understand the role of science, biology, and technology as they relate to neuroscience and drug abuse and addiction research. There is a lack of public understanding of behaviors that increase the risk for drug abuse, the use of animals in drug abuse related behavioral and biomedical research, and the necessity for basic research to make progress toward improving health. Furthermore, there is a substantial misunderstanding about the nature of addiction as a biologically based brain disorder. To address all of these issues, it is imperative that efforts be made to educate our nation's school children, the general public, health care workers, members of the judicial system, and other groups about the science of addiction.

Therefore to address these issues this contract solicitation seeks innovative projects or programs that will substantially improve scientific literacy among one or more of the following groups: 1) students and teachers at the kindergarten through 12^{th} grade levels; 2) the general public; 3) health care practitioners; 4) members of the judicial system; 5) other groups

that have a need to be scientifically literate. Programs or projects must seek to improve general scientific literacy with a specific focus on drug abuse related research. For example, a project could teach basic neuroscience first and then subsequently teach how abused drugs act in the brain and body. Programs and projects aimed at school children should convey the scientific process in a way which makes learning science fun and interesting for the students and which captures their enthusiasm for science. Student programs and projects must also adhere to the National Science Education Standards. Programs or projects aimed at other groups should be directed to increasing their knowledge of scientific terms, concepts, reasoning, and their ability to understand scientific public policy issues. Regardless of the intended audience, all programs and projects must include an evaluation component that can provide useful and accurate information on the efficacy of the program or project.

Phase I should include studies to determine the best format for the chosen audience (e.g. focus groups), studies that demonstrate feasibility, and the development of a prototype.

Phase II should include continued formative evaluations to guide the development of the program or project, development of the program or project, and a summative evaluation to determine the project/program's efficacy in improving science education/literacy.

030 Medicinal Chemistry - Design and Synthesis of Treatment Agents for Drug Abuse
(accepting Fast Track proposals)

The purpose of this contract is to design and synthesize compounds that moderate the effects of cocaine or methamphetamine. Examples are compounds which affect primarily dopaminergic systems and would either represent "agonist type" therapies for cocaine, antagonize cocaine's effects, or prevent relapse. Compounds active at the D1 and D3 receptors are of special interest. Phase I would be used to design and synthesize new entities as possible treatment agents for cocaine or methamphetamine abuse. Phase II would be used to further develop these entities into clinical candidates for the treatment of cocaine or methamphetamine abuse. The Contractor may carry out their own *in vitro* or *in vivo* pharmacological screens, or may use the NIDA Cocaine Treatment Discovery Program screens (in vitro binding studies, rodent locomotor activity studies, rodent and primate drug discrimination studies, and rodent and primate self-administration studies). During Phase II, the Contractor may independently develop new treatment entities, or may request to enter into a cooperative agreement with NIDA for the further development of a new drug with commercial promise as a treatment agent.

032 Dosage from Development
(accepting Fast Track proposals)

NIDA is seeking SBIR contract proposals on innovative and novel dosage form development for the pharmacotherapy of substance abuse and addiction such as opiates, stimulants (cocaine and methamphetamine), and tobacco. The classes of pharmacotherapeutic agents include opioid-receptor agonists/antagonists, dopamine-receptor agonists/antagonists, serotonin-receptor agonists/antagonists, monoamine transporter agonists, antimanic agents, anti-smoking agents and immunogenic therapies (antibody products to reduce peripheral levels of drug substances).

In Phase I, the contractor is expected to demonstrate the feasibility of the dosage form by formulating a prototype dosage form of a medication with potential for pharmacotherapeutic applications in addiction that is physico-chemically stable and has adequate *in vitro* release and/or *in vivo* bioavailability. In Phase II, the contractor is expected to provide GMP scale-up of the formulation of a stable dosage form with acceptable *in vitro* and *in vivo* bioavailability in animal models or in humans. The contractor is also expected to demonstrate the preclinical safety and efficacy of the formulation.

034 Develop New Technologies for Drug Abuse Prevention Delivery: Translation of Empirically Validated Prevention Strategies and Programs into New Technologies
(accepting Fast Track proposals)

The past several years have witnessed considerable interest in using technology in educational settings with children, youth, and adults. New technologies, including CD-ROM, the Internet, videotape, videodisc, and other electronic means have great potential for delivering and disseminating drug abuse

prevention programs. However, the application and development of such technologies has lagged behind their use in other settings and contexts. These new technologies potentially provide a more cost effective way of delivering prevention services.

Previous PRB SBIR contracts have focused on prevention research dissemination (mechanisms which are utilized to transfer drug abuse prevention information to practitioners, policy makers, and the public) and measurement modules for prevention interventions (aiding various groups to identify existing or develop new measures of the antecedents, mediators and outcomes thought to be associated with the interventions). This solicitation seeks to take programs with proven efficacy and translate research to practice through the use of new technologies.

Phase I would explore the practicality of technological solutions to the delivery of drug abuse prevention programs. Selected technical approaches would be developed and pilot tested. One could take a proven prevention program and place it into a new technology. Phase II would witness further development and the testing of these technologies in applied clinical (i.e. prevention) settings including further developing those technologies that were successfully pilot tested in Phase I.

037 Novel Drug Delivery System for the Mouse

The availability of administering drugs to animals in a manner that more closely reflects the way in which humans self-administer drugs would be valuable. Moreover, indwelling cannulae pose several problems including survival of surgery, animal restraint, cannulae patency, etc. Such problems prevent high-throughput screens for mutations and therapeutics in mice that affect the responses to drugs of abuse. Development of inhalation self-administration for example would provide a more relevant means of studying agents abuse by inhalation, especially in mice. Modeling human drug abuse (of cocaine, heroin and nicotine) in animals requires rapid delivery of the drug. The rate of drug delivery can influence the reinforcing effects of the drug. In addition, rapid delivery of (drug) reinforcers facilitates conditioning of an instrumental response. *To be useful for this purpose, the rate of drug delivery with a new device should approximate rates via intravenous injection or achieved by inhalation*. Otherwise, the device would be of no more utility than current methods for studying drug self-administration in animals without surgical preparation, e.g. oral consumption. Thus, the delivery system should require little or no surgery. The device might deliver a drug transdermally or might deliver the drug in volatilized form. Other innovative methods are encouraged. Phase I application should demonstrate the feasibility of the method of delivery for one or more drugs of abuse. Phase II would finalize development of the device, including testing on a wide range of laboratory mouse species and physiological and behavioral comparison with other methods of delivery.

041 Functional Imaging Agents
(accepting Fast Track proposals)

Imaging at both the cellular and organ level has greatly advanced our understanding of the biological processes associated with the effects of substance abuse upon the brain. A need remains, however, for new and improved imaging agents which reveal function, increase the repertoire of molecules which may be studied, and offer improved quantification of observations. This solicitation requests development of such agents, particularly for use in functional magnetic resonance imaging and micro PET studies in animals.

042 Technologies for Localizing Gene Expression and Proteins in the Nervous System

Classical methods for localizing the expression of mRNA transcripts and proteins in tissue use *in situ* hybridization, immunohistochemistry, and serial reconstruction. These methods are impractical for the simultaneous and rapid identification of the location in three-dimensional space of over 30,000 genes expressed in the nervous system and their cognate proteins. This announcement solicits applications for the development of physical-chemical and computational methods that would permit the simultaneous localization of thousands of proteins and transcripts in three-dimensional space. Phase I would test the feasibility of the methods to be used. Phase II would apply the method to the localization of proteins and transcripts in the mouse nervous system.

043 Activity-based Protein Profiling

The discovery of protein function would be greatly accelerated by characterizing proteins based on changes in their activity. This announcement solicits applications for chemical synthesis and development of active-site probes for visualizing the function and expression of an entire class of proteins or enzymes. Phase I applications should demonstrate the feasibility of the chemical synthesis of the active site probes. Phase II should develop a final product that can be used by NIDA investigators.

044 High-throughput screening of functional activity of proteins using biosensor-based technology

The field of proteomics would be significantly advanced if uncharacterized gene products could be rapidly screened for functional activity. This announcement solicits applications for biosensor-based or mass spectrometric methods to conduct high-throughput screening of proteins for particular binding properties. This method may be base on any existing biosensor or mass spectrometric technology. Phase I applications should demonstrate the feasibility of the proposed method for detecting one or more specific interactions. Phase II should develop a prototype suitable for high-throughput screening.

045 Develop Methodologies for Cost Analysis of Substance Abuse Prevention Programs

States, community organizations, schools and other local agencies are under increasing pressure to document the cost-benefit and cost-effectiveness of their prevention efforts. In the current, cost-conscious environment, there is a need to demonstrate that an investment in prevention can lead not only to significant reductions in the prevalence of drug use, but also a reduction in public expenditures in such areas as Medicaid, welfare, criminal justice, treatment, lost wages, etc. While there are efforts under way to do these types of analyses, there are no uniform approaches to either cost-benefit or cost-effectiveness analysis, nor is there very much expertise at the local level to accomplish this. In addition, the methods that do exist tend to be more one-time, research-oriented evaluations that are costly, require considerable data collection and are, thus, difficult for a public agency to do on an on-going basis. Further, while most of the cost analyses currently under way focus on treatment, it is much more difficult to evaluate cost-benefit and cost-effectiveness of prevention programs.

This initiative is designed to encourage the development of standard, lower-cost approaches to cost analysis that can be implemented across states, communities and prevention settings that will rely on the use of management information systems (MIS) and administrative data rather than on client interviews. In this way, systems can be developed that gather needed data on clients without the costly use of repeated interviews or assessments or the need to continually track clients' whereabouts. The MIS data would be based upon on-going information kept by the service agencies (e.g., on program costs, client attendance rates) and schools (e.g. grades, drop-out rates, attendance). The administrative data would also be derived from state files on local drug prevalence and treatment needs, Medicaid, welfare, criminal justice, and employment.

Phase I could have elements of: (1) cost program development and implementation, (2) sustainability cost, (3) availability of administrative data in communities and schools, and (4) creation and pilot testing of methodologies for cost analyses based upon available data that can be packaged and adapted to the needs of specific states, communities, or schools.

Phase II would involve the actual testing of the methodologies across various communities. Criteria for success would include methodologies that can be used with data generally available across communities, actual cost-benefit and cost-effectiveness measures that reflect both program costs and outcomes, and outcome measures that are relevant and useful to the communities and can be integrated into their own information systems. Phase II should also include the development of a manual to help communities implement such cost analysis systems.

046 Develop Prevention Services Analytic Tools for Improved Substance Abuse Prevention Delivery

Significant research has occurred regarding individual prevention programs including their efficacy, effectiveness, processes, and outcomes. However, relatively little has been

accomplished as regards the application of prevention services analysis to improve the climate for and optimize the delivery of prevention programs. Prevention services include factors that influence the availability, accessibility, and utilization of prevention services as well as how these services are organized, financed, delivered, and utilized.

Instruments/tools are needed to aid prevention policy makers and practitioners in developing a community profile priori to the selection, adaptation, and implementation of research programs and strategies in order to maximize their prevention efforts. These instruments could assess prevention demand, availability of existing programming, barriers, incentives, policies, financing, organization, dissenting views, linkage, management, effectiveness, etc. so as to present information that would permit prevention professionals to optimize the delivery of prevention services.

The primary purpose of the Phase I contract would be to conduct studies to develop or determine the availability, validity and reliability of a wide variety of measures for use in communities with different services profiles. Toward this end, the Contractor would catalog existing measures and data sets in the public domain that could be used to conduct services studies. Some development and pilot testing of an instrument would also be beneficial. Instrument design and form are left to the Contractor's discretion and could be simple paper and pencil, CD-ROM, internet, etc.

Phase II would involve a series of controlled studies of the different measures and device (i.e. tool/instrument) identified in Phase I plus any relevant additional items. The Contractor should develop via paper and pencil methods as well as methods that use computers, telephones and the internet, instruments that produce useable databases for the target audience. The Contractor should also provide the necessary software for analyzing these databases that provides meaningful analysis and output for the end user.

047 Develop and Maintain Substance Abuse Prevention Methodological Software

Software development is crucial to prevention research. It permits the testing of new methods, their dissemination, makes a substantial impact upon the field, and permits feedback from the scientific community. Producing good software is time consuming and complicated. Providing software development and maintenance support to the scientific community will enable researchers to focus their energies on prevention research. This solicitation is fueled by the enormous growth of the Internet and WorldWide Web which makes this effort even more important and cost effective.

Phase I could see the development and pilot testing of at least one analytic technique and that technique's placement on the Web for all to use. These should be cutting-edge methods that are not available in any of the major commercial statistical packages. Phase II would see the development, testing, and final product of additional prevention research analytical/methodological techniques. These products should include graphical user interfaces, documenting the software, packaging it for distribution on the web, and maintaining the software by fixing bugs, answering questions, etc. Also included should be developing and maintaining websites for public use where people can download software, manuals, tech reports, look at FAQ pages, and so on. User support is a must.

048 Virtual Reality for Treatment of Pain *(accepting Fast Track proposals)*

Recent findings (Hoffman et al., 2000, Pain, 85, 305-309) have suggested that Virtual Reality (VR) exposure can reduce reported pain during wound care. Proposals are sought to examine the utility of VR technologies in the treatment of various types of pain. Development of treatments for both acute and chronic pain is sought. These treatments can be based in clinical settings or the patient's homes. Phase I testing should establish the feasibility of the use of this technology in the particular population to be tested. Phase I should also produce data that demonstrates that this methodology is effective for the particular type of pain being treated. Phase II should involve larger-scale testing (e.g. more subjects and treatment trials) examining various treatment parameters (e.g. timing of treatment, types of VR environments). The focus of Phase II testing should be the refinement of this treatment for use in pain patients.

049 Virtual Reality for the Treatment of Drug Abuse
(accepting Fast Track proposals)

Recent findings (Hoffman et al., 2000, Pain, 85, 305-309) have suggested that Virtual Reality (VR) can be a useful clinical tool. In this particular study, VR exposure was used to allow patients to selectively not attend to an otherwise painful procedure. Drug abuse, like pain, is a problem that is strongly impacted by stimuli in the abuser's environment and psychological factors. Thus, it is reasonable to assume that VR may be useful in allowing individuals to ignore drugs cravings, withdrawal symptoms or environmental cues that promote drug abuse. Proposals are sought to examine the utility of VR technologies in the treatment of various types of drug abuse. These treatments can be based in clinical settings or the patient's homes. These treatments can be developed to address drug withdrawal, drug craving or on-going drug related behaviors. The development of VR technologies to address abuse of all types of drugs (e.g. cocaine, marijuana, nicotine, alcohol, inhalants) are sought. Phase I testing should establish the feasibility of the use of this technology for the particular drug problem addressed (e.g. cocaine craving, opioid withdrawal) and should also produce data that demonstrates that this methodology is effective for the particular drug problem. Phase II should involve larger-scale testing (e.g. more subjects and treatment trials) examining various treatment parameters (e.g. timing of treatment, types of VR environments). The focus of Phase II testing should be the refinement of this treatment for use in the treatment of drug abusers.

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES (NIEHS)

Human health and human disease result from three interactive elements: environmental exposures, individual susceptibility and time. The mission of NIEHS is to reduce the burden of human illness and dysfunction from environmental exposures by understanding each of these elements and how they interrelate. NIEHS achieves its mission through multidisciplinary biomedical research programs, prevention and intervention efforts, and communication strategies that encompass training, education, technology transfer, and community outreach.

This Solicitation invites proposals in the following areas:

084 Development of Clinical Resources for Toxicogenomic Studies

In order to translate the revolution in technology related to toxicogenomics to improvements in human health, human tissues from well-characterized populations with well-characterized exposures are needed.

The goal of this project is to acquire and make available to researchers clinical samples from human populations in areas of high environmental pollution. The cryopreserved samples (e.g. tissue, blood, serum, and fluids) must be related to an extensive record of biological data (point of origin, clinical/disease phenotype, family history, exposure assessment etc). Ideally, health effects in children born to exposed mothers (child-mother phenotypes) would be particularly useful. Such matched records/samples should allow the determination of birth outcomes, developmental milestones, adverse drug reactions, overall health status, extent of maternal exposure, extent of fetal exposure and genotypes.

These records/samples should be appropriate for genotyping polymorphisms of genes determining or influencing disease susceptibility, and for gene expression analyses. Access to these samples and records could be made available to researchers on a contract or purchase basis.

085 Development of Surrogate Biomarkers of Exposure or Toxicity

A number of technological and conceptual advances in molecular biology and medicine, genetics and genomics have opened significant opportunities for the development of new tissue specific surrogate biomarkers. A surrogate biomarker is an endpoint measurement that allows the monitoring of the activity of a particular tissue and, therefore, would be helpful in determining tissue specific damage by virtue of alterations in its level or activity. The purpose of this initiative is to solicit the development and validation of new surrogate biomarkers that would be indicative of either exposure to a specific chemical or class of chemicals and/or of tissue or organ-specific damage that can be measured either noninvasively or from a serum, meconium, urine or saliva samples. Surrogate

biomarkers can be developed for any organ or tissue such as the liver, kidney, heart, reproductive system, immune system, central nervous system etc. One possible approach would be to screen all the tissue specific genes that have signal sequences as they are likely to be secreted from the tissue and thereby may be a possible biomarker of that tissue's activity. The surrogate biomarkers must be easily measured, be specific and reliable, and must be validated against known tissue toxicants.

086 Development of Predictive in vitro Tests for Toxicity Testing

The NIEHS is interested in developing in vitro test systems that provide quantitative estimates of the systemic toxicity potential of chemicals and that identify the critical target organs involved. Such systems, as part of an integrated battery would be used to estimate the relative toxicity of chemicals by providing information on susceptible organ systems and toxicokinetic parameters. To this end, we solicit the development of cell cultures that mimic cell activity in vivo including culture systems that can provide metabolism data and/or kinetic information across tissues such as the intestine and blood brain barrier. With the advent of gene expression analysis using microarrays it is possible to assess gene expression in cells in culture and cells in vivo and to then devise methods to make the cell cultures mimic the in vivo situation at least with regard to gene expression. This can also be done for proteomics. It is anticipated that the results of this project would be cell cultures that would, because of their similarity to the cells in the animal, be useful to be used as screens for toxicity assessment. Cells can be human or animal derived but should be amenable to alterations in growth rate in culture so that toxicity can be assessed in static, differentiated and growing cells. Cell cultures produced under this initiative should also be validated, using tissue specific toxicants, in order to confirm that the in vitro response matches the known response in the intact animal. Note that the development of any form of skin cultures cannot be proposed for this initiative.

087 Development of Novel Approaches to Proteomics

Now that the human genome has been mapped, attention is beginning to turn to the characterization of the proteome, which is the global protein profile reflecting cellular activity in relation to time, development, and interaction with the environment. Proteomics is the analysis of the proteome, and the current paradigm is based on separation of components by 2-dimensional gel electrophoresis, followed by protein identification based on mass spectrometric analysis of digests of the protein gel spots. This combination is laborious and relatively insensitive to low level proteins. Thus, there is a significant need for new approaches to proteome characterization, such as affinity-and or chip-based techniques and/or new approaches to enrichment, detection and characterization of post-translationally modified proteins. Thus the NIEHS is soliciting proposals that address the need for high throughput, high sensitivity proteome characterization.

088 Development of cDNA Arrays for Male Reproductive Toxicology

The cDNA microarrays currently available are of limited use for male reproductive toxicology because they lack testis specific genes. The testis, and particularly the developing germ cells, contain many uniquely expressed genes and cell-type specific alternative transcripts. Thus the purpose of this initiative is to either develop or identify available ESTs representing genes expressed in the mouse testis (somatic and germ cells) to verify, the identity of these ESTs and to select those testis specific genes that are unique or have low homology to sequences of known genes. These would be used to develop testis specific cDNA microarrays (5-10,000 genes) that would be tested and validated with regard to quality, specificity and completeness of the genes arrayed. For the purpose of this initiative, either the cDNAs themselves, the complete microarrays, or both could be developed as the product.

NATIONAL INSTITUTE OF MENTAL HEALTH (NIMH)

The mission of the National Institute of Mental Health (NIMH) is to diminish the burden of mental illness through research. To achieve this goal, the NIMH funds basic research, clinical studies, and services delivery research concerning any aspect of behavioral and mental disorders (including HIV prevention and neuro AIDS research). Ultimately, this research will lead to greater understanding, better treatment

and rehabilitation or prevention of mental disorders. The NIMH is also concerned with the speedy dissemination and use of this knowledge through scientific communications and public education, and in its more effective implementation in practice and service delivery systems.

This Solicitation invites proposals in the following areas:

027 Neuroscience-based Cognitive Tests as Outcomes Measures Project

The purpose of this contract is to develop outcome measures for clinical trials of depression, dementia or schizophrenia that are based on state-of-the-art neuroscience- based tests and methods. Current cognitive outcome measures that are used in trials are based on old-style traditional clinical methods. Because the Food and Drug Administration does not require these advances, typical clinical trials have not included novel tests. Newer models of cognition have informed the design of basic neuroscience/neurocognitive research and these methods can now be applied to clinical trials.

The need for this activity was expressed by participants at the NIMH sponsored workshop "Neurocognitive Outcome Measures in 21st Century Clinical Trials: Advancing the Translation of Cognitive Neuroscience" held in Bethesda on June 25-26, 2001.

It is assumed that theses tests would be used as outcomes in multi-site clinical trials of putative medications, which will require the ability for repeated-use over time. Thus, issues of administration and inter-site variability must be completely addressed. In addition, there is the need for data to be accurately transferred from sites to a central data-center. Whether the test either is computer-based or uses paper-and-pencil methods, the scoring system should be computer-based and allow sites to send data to the central data-center and for the center to send updates to the site PC. Finally, a standalone, single site version should be produced.

Tests that are warranted might include those that tap working memory, aspects of attention, visual and auditory learning, or language function (other than traditional assessments of fluency or vocabulary). It is likely and desired, but not required for the test to be computer-based. More than one test can be developed. Ease of use should also be considered so that the product is not unnecessarily irritating or unappealing to the test-taker. The final product might include:

- An analysis and justification for development of the neuroscience-based test(s)
- Manual for training and administration
- An operable version of the test (PC-based or paper and pencil) with multiple forms for repeated use (when needed) that is user-friendly
- Establishment of reliability (test-retest, internal consistency) in appropriate samples
- Establishment of concurrent validity with the original neuroscience-based test
- Establishment of resilience to repeated use (freedom from excessive practice-effects)
- Development of a computer-based scoring and data-transfer system. This could be formatted so that sites are not allowed to see the scored data, only to transfer it to the data center. Alternatively, sites would be able to score data
- The system should be able to operate on Windows (95 or higher) and Mac OS (system 8.1 or higher)
- The test data should be easily exportable to both SAS, SPSS, and Microsoft Excel
- Ideally, a version of all materials, including the training manual and test should be produced for Spanish-speaking individuals with appropriate reliability established

028 Web-based Resource on Use and Development of Cognitive Neuroscience-based Tests in Clinical Trials

The purpose of this contract is to develop a web-based resource for researchers that can be used to assist in the development and use of cognitive neuroscience-based test in clinical trials. Current cognitive outcome measures that are used in trials are based on old-style traditional clinical methods. Because the Food and Drug Administration does not require these advances, typical clinical trials have not included novel

tests. Newer models of cognition have informed the design of basic neuroscience/neurocognitive research and these methods can now be applied to clinical trials. Overall, these tests will help scientists better understand how treatments affect the brain and how the brain functions when being treated.

A web-based resource can allow developers, researchers, and trialists to share information, avoid common pitfalls, and further advance the use of state-of-the-art measures in clinical trials. It also can serve to motivate researchers to develop these measures further.

Content might come from:

- Relevant published articles (available as links from Medline, Acrobat files, etc.)
- Abstracts from symposia and presentations and meetings
- Information on upcoming relevant meetings
- Resources for funding
- Links to test developers, cognitive neuroscience researchers, and clinical trialists who use these methods

Examples of content may include:

Cognitive-neuroscience section (material that is relevant to cognitive neuroscientists): Should include listings and links to tests that might be used, articles on practical issues of modifying a test into one that can be used in clinical trials, clinical trials primer and links.

Clinical trialists section: Q&A for use of cognitive neuroscience tasks, links to cognitive-neuroscience researchers, practical issues on choosing cognitive tests, rater training, establishing reliability and validity.

Given the infancy of this process, some content will need to be generated for the site.

The contract would be to establish a plan for this website in terms of content, approaches to use, acquisition, storage, and revision of content, and a system for access, sharing, and distribution.

The need for this activity was expressed by participants at the NIMH sponsored workshop "Neurocognitive Outcome Measures in 21st Century Clinical Trials: Advancing the Translation of Cognitive Neuroscience" held in Bethesda on June 25-26, 2001.

029 Mental Health Intervention Trials Operational Archive Project

The purpose of this contract is to develop an archive of operational experience in larger-scale, particularly multi-site, intervention trials in mental health. As the field moves to larger, longer, more complex studies, it seems as though a set of issues needs to be independently discovered and solutions need to be independently invented each time a study is begun. Examples of these issues include:

Structural: how should trials be organized; what functions should be centralized; what committees need to be established; how are disputes resolved; who has rights to data and when; should the data be archived for public use and when

Operational: how are raters trained, reliability established and maintained; are there manuals and training tapes available and how should they be used; are the newer web-based approaches usable; how is site variability minimized; how is consent maintained over the long term; what are special operational challenges in non-academic settings

Practical: how should data safety and monitoring be carried out; what standard for conflicts of interest should be established; what incentives can be provided to sites and investigators for participation; should industry participation be invited; how to handle trial completion, open continuation, compassionate use

The contract would be to establish a plan for this archive in terms of content, approaches to investigators, database acquisition, storage, and retrieval, and a system for access, sharing, and distribution.

The need for this activity was expressed by participants at the NIMH sponsored workshop "Neurocognitive Outcome Measures in 21st Century Clinical Trials: Advancing the Translation of Cognitive Neuroscience" held in Bethesda on June 25-26, 2001.

030 Families as Research Partners: Development of Interactive Educational and Dissemination Modules to Train Family Members of Children with Emotional or Behavioral Disorders about Mental Health Research Methods, Procedures, Data Analyses, and Interpretation
(accepting Fast Track proposals)

The purpose of this contract is to train families of children with emotional or behavioral disorders on research issues relating to studies on service delivery, treatment development, preventive interventions, risk reduction, or epidemiology. Because families are pivotal members of any treatment or intervention team, offering unique perspectives on their child's functioning and response to interventions, it is important that they be involved fully as partners in intervention development and delivery of care. Often this is not the case, particularly with minority families for whom there may be additional cultural, language and economic barriers.

Anticipated outcomes include encouraging the development of training materials and the testing of models for involving families fully as research partners in a range of studies on child and adolescent mental health, behavioral or emotional disorders, and service delivery. Particular attention and sensitivity should be paid to developing appropriate materials and strategies to engage underserved minority families in this process. Modules are needed to address issues such as:

- random assignment and its ethical and scientific implications
- research design and development of new models of care
- ethical issues in validating treatment or preventive interventions
- research partnerships and the delineation of roles
- health care and studies of system variables
- identification, recognition and clinical issues in assessment and diagnosis

Reports that are relevant to this announcement include:

Blueprint for change: Research on Child and Adolescent Mental Health: A report of the National Advisory Mental Health Council, May 2001

Surgeon General's National Action Agenda for Children, January 2001

Bridging Science and Service: A report of the National Advisory Mental Health Council

031 Development of Integrated Statistical Software for Longitudinal Community-based Clinical Trials

While the safety and efficacy of treatments can be tested in tightly controlled clinical trials, questions of effectiveness, applicability, acceptability, and preferences must be answered in community settings, where investigators have little control of many factors. Particularly in longitudinal community-based clinical trials and naturalistic studies, data for individuals at particular time points will be missing, assessments made over time are likely to be irregularly spaced, subjects are likely to be nested within clusters (such as treatment settings, schools, or neighborhoods), data will be correlated over time for the same individual, desired outcome variables may be ordinal instead of interval, outcome variables may have nonnormal distributions or require multiple respondents, and missing data is likely to be nonrandom.

Statistical procedures for these problems, those in measurement (e.g., IRT), and those to adjust effect estimation for group assignment biases (e.g., propensity scores) have been developed. Inclusive, user-friendly, computer software packages with sophisticated graphic capabilities that incorporate flexibility in specifying models for mental health clinical trial and naturalistic data have not.

This SBIR contract is designed to support the development, updating, and/or consolidation of software tools for this purpose. This tool should include the software, extensive documentation for statisticians (with examples and graphics), a help-line and/or Internet site, and a primer for nonstatisticians on each of the methods included in the package. The primer needs to be developed in conjunction with clinical, social and behavioral science, and health services researchers.

032 Development of Dissemination Tools for the Delivery of Empirically Validated Interventions in Rural and Frontier Areas

The purpose of this SBIR contract is to develop and market effective dissemination tools for the delivery of empirically validated interventions by mental health providers in rural and frontier areas. This initiative is in response to recommendations put forth at the NIMH Conference on Rural Mental Health Research: Charting A Future Course.

The nearly 60 million Americans living in rural and frontier America have the same kinds of mental and general health problems as individuals who live in urban and suburban areas. However, in addition to access barriers that affect all Americans, rural areas have unique characteristics that may further limit receipt of appropriate services. There is widespread poverty, poor road conditions and little public transportation. Other barriers may be culturally related to the extent that rural America still reflects a different set of values and lifestyles than urban America. There are language barriers for those who cannot speak or read English and physical obstacles for those with disabilities. In addition, the stigma of mental illness along with the lack of confidentiality and anonymity in small-towns often prevent many residents in need of care from seeking services. To address these barriers, mental health providers require this information to provide effective and appropriate mental health services in rural and frontier communities.

In addition, although much has been learned about the mental health problems and needs for services for individuals living in rural and frontier America, this information has not be transmitted to mental health providers in these areas. For example, intervention programs designed for urban areas may not be appropriate for effective delivery of rural mental health services. The development and marketing of dissemination tools would help to avoid inappropriate implementation of mental health programs not tailored to rural and frontier areas.

033 Minor Offenders with Severe Mental Illness: Developing an Educational Module to Foster Collaboration between Mental Health and Criminal Justice Staff

The purpose of this SBIR contract is to develop an educational tool that promotes cross-systems understanding and fosters improved collaboration between mental health and criminal justice personnel concerning minor offenders with severe mental illness. This initiative is in response to recommendations put forth at the NIMH/MacArthur Foundation Workshop: Future Research on Mental Health Courts and Other Jail Diversion Strategies: Setting an Agenda/Building Partnerships.

The number of people with severe mental illness who come in contact with the criminal justice system for minor offenses is significant, and the intersection of mental health and criminal justice services for these individuals can be complicated. Cross-systems interactions occur at a variety of levels, though, given no formal guidelines, the parameters of such interactions are likely to vary widely. Under such circumstances, achieving mental health goals may be maximized by making those goals explicit and understood by all involved. There is significant empirical evidence concerning symptoms, severity, treatment, history of illness, and the importance of community and psychosocial components that can contribute to more effective case management and with which those providing criminal justice services may be unfamiliar. Knowledge of this evidence may facilitate more effective, collaborative service planning. From the mental health workers' perspective, ethical concerns relating to coercive criminal justice strategies and possible aversion to working with involuntary clients may be lessened by delineation and mutual understanding of the mental health strategies and concerns, and improved mental health/criminal justice collaboration. Finally, given the importance of preserving client trust and working-relationship with both systems, consideration must be given to delineating the nature and extent of the collaboration to the client and, where appropriate, to the client's family. (Draine and Solomon, 2000)

The goals of this SBIR contract are to develop an innovative educational module for criminal justice personnel and mental health staff that 1) conveys the empirical evidence on: types and course of severe mental illnesses, their proven

treatments, and the kinds of community services and interventions that maintain treatment adherence and improved outcomes. Development of this module must lead to a product that will be understandable, useful and acceptable to criminal justice staff at a variety of levels, and 2) provides preliminary guidance to collaborators for specifying the parameters of the mental health/criminal justice collaboration. This might include outlining processes to define criteria for: hospitalization, threats of incarceration, actual incarceration, and for identifying and obtaining consent for the release of specific information between and outside of (e.g., to family) the collaborating parties.

The products created under this contract should be developed for and tailored to the particular targeted audiences based on assessment of their needs. Input from experts and front-line workers in the fields of mental health and criminal justice should inform the content of the modules, and the contractor must show capability of working with such persons. Suggestions for mediums and strategies of dissemination should be included, however, the development of these would occur under a future contract.

034 Develop Approaches for Dissemination of Proven Mental Health Intervention Programs for Youth to Schools and Community Based Programs: Addressing the Challenges of Identification, Fidelity, Cost-effectiveness and Sustainability

There are a number of youth-focused interventions with proven effectiveness for reducing a number of negative outcomes; early aggressive behavior; poor adjustment post divorce; poor adjustment post parental death. Many interventions are school or community based. The challenge to these settings are 1- finding appropriate effective interventions to implement (e.g., teacher-focused; parent-focused); 2- implementing proven interventions with fidelity (develop training tools, such as videos, training approaches); 3- determining cost-effective approaches to evaluating the programs to see if they should continue in their communities; 4- sustaining programs that are effective. This SBIR contract would solicit approaches for disseminating proven intervention programs with these challenges in mind.

035 Development of Tools for the Assessment of Depression

The purpose of this SBIR contract is to develop effective tools for the assessment of depression. More specifically, particular emphasis is placed upon measurement of the cognitive, affective, and behavioral components of depression. Historically, diagnostic measures of depression have been of two kinds: patient self-report of symptoms or clinician rating of patient symptoms based on clinician observation and patient self-report. These measures have been widely used for multiple purposes with broad public health implications, including validation of the utility of new medications for treatment and identification of candidates for various treatments of depression. However, they have failed to target specific symptom expression and instead have offered global indices of depression. Recent advances in understanding the nosology and pathophysiology of depression herald a call for the development of new tools for assessing its components. For example, laboratory and behavioral tests have demonstrated abnormalities in neurotransmitter and neuroendocrine functioning. Polysomnographic techniques have identified sleep pattern disruption in depressed individuals. Functional and structural brain imaging techniques have identified abnormalities in brain function associated with depression. Behavioral experiments have increased our understanding of cognitive and affective processing in depression. These new advances have highlighted a growing realization that depression is not a single entity, but rather a heterogeneous complex of disorders. The capability of assessment tools to deal with such heterogeneity is needed for at least two reasons. First, different forms of depression may respond differentially to various treatment modalities, or have a different course. Second, the completion of the human genome raises the possibility of relating disorder subtypes to specific genetic vulnerabilities; however, refined measurement is a prerequisite to conduct the studies that can link genetic diatheses to particular forms of disorder, and to guide the precise tailoring of therapeutics that will be possible in the future.

The products created under this contract should be developed for and tailored to a wide audience of consumers. Specifically, products, or families of products, should be culturally appropriate and valid for individuals at varying stages of development (i.e., children, adults, elderly). The

contractor should be capable of working with experts in the field of mental health (in particular, behavioral scientists, cognitive neuroscientists, psychometricians, and statisticians). The tools developed should be appropriate for use in diverse settings including clinical trials based in academic centers and community-based mental health centers. Adequate sensitivity, specificity, reliability, and validity should be demonstrated, and the development approach should reflect current state of the art in measurement theory.

Assessment tools might take the form of laboratory tests, observation, or patient self-report. Assessment tools might address validated components of depression such as: depressed mood, hopelessness, psychomotor retardation, sleep disruption, fatigue or loss of energy, diminished ability to think or concentrate, disturbed self-image (i.e., feelings of worthlessness or excessive guilt) or suicidal ideation. Strategies might include the development of a single tool or the development of a battery of tests that could be used together to identify the cognitive, behavioral, and affective components of depression that represent targets for treatment.

036 Addressing Mental Health Needs of Victims of Disasters and Trauma
(accepting Fast Track proposals)

The purpose of the SBIR contract is to develop and maintain a web site for health, education, and justice professionals as well as families about effective and promising strategies for addressing the mental health needs of victims/survivors of disasters and mass trauma; and to facilitate collaboration between research investigators and service providers to pursue new research opportunities. The National Institute of Mental Health (NIMH) has been supporting and conducting research on emergency and disaster mental health for several decades. Most recently, NIMH has been working with several federal agencies (the U.S. Department of Health and Human Services, Center for Mental Health Services, Emergency Services and Disaster Relief Branch (and the Federal Emergency Management Agency), the U.S. Department of Education, Safe and Drug Free Schools Program, and the U.S. Department of Justice, Office for Victims of Crime) on a series of activities to integrate evidence–based information into the federal, state and local mental health response to disasters and mass traumas.

Recent nationally reported school shootings such as those that occurred in Bethel, Alaska; Pearl, Mississippi; West Paducah, Kentucky; Jonesboro, Arkansas; Edinboro, Pennsylvania; Springfield, Oregon; Littleton, Colorado; Santee, California; and other locations have shocked the country. Many questions are being asked about how these tragedies could have been prevented, how those directly involved can be helped, and how we can avoid such events in the future. Helping young people avoid or overcome emotional problems in the wake of violence or disaster is one of the most important challenges a parent, teacher, or mental health professional can face. Each year many children and adolescents sustain injuries from violence, lose friends or family members, or are adversely affected by witnessing a violent or catastrophic event. Each situation is unique, whether it centers upon a plane crash where many people are killed, automobile accidents involving friends or family members, or natural disasters such as earthquakes, floods, or hurricanes where deaths occur and homes are lost—but these events have similarities as well, and cause similar reactions in children. Even in the course of everyday life, exposure to violence in the home or on the streets can lead to emotional harm.

The purpose of this web site is to make available information about the impact of violence and disasters on children; offer best practice guidance for screening, assessment, crisis response, triage care, specialty treatment strategies to minimize long-term emotional harm and facilitate recovery; and facilitate new community-based research activities. Currently, there is no single source for credible evidence-based guidance on approaches to addressing the mental health needs of victims/survivors that is targeted to a variety of audiences (emergency personnel, disaster mental health workers, school personnel, law enforcement, mental health providers, parents, etc.). Additionally, there are limited opportunities for researchers and service providers to discuss collaboration on real-world research projects that may improve our understanding about effective screening and early intervention strategies. The web site should be innovative in its use of appropriate web technology (e.g., creative/appropriate use of interactive forms, multimedia) as an educational tool. The web site would need to be maintained with current information. A number of other government agencies provide web-based resources on emergency and disaster mental health and this web site would need to

have appropriate and accurate links to those sites when these other sites have been identified as credible sources of information. This contract would also need to include the development of marketing strategies to effectively promote and evaluate the web site: monitor and assess its usefulness (level of interest, knowledge level); usability (navigation, format); and dissemination among intended audiences. A multi-disciplinary approach to this contract is encouraged. Potential contractors should be able to work with experts in the fields of mental and allied health care (social psychology, behavioral science, educational psychology, managed care providers), law enforcement/justice, and education.

037 Resources for Physical Injury in Child Abuse
(accepting Fast Track proposals)

The National Institute of Mental Health and the Centers for Disease Control and Prevention co-sponsored a research conference on physical injuries in child abuse. The purpose of the meeting was to review current description and coding of injuries, acts, and injury consequences associated with physical abuse of children and adolescents and to discuss research that is needed to more adequately describe and code inflicted physical injuries in child abuse cases. (see **http://www.nimh.nih.gov/childhp/abuseinjuries.cfm**) It was held March 29-30, 1998 on the NIH campus in Bethesda, Maryland. This multidisciplinary meeting brought together experts in child physical abuse, including pediatricians, neurologists, radiologists, pathologists, and psychologists. Participants discussed terminology necessary to discuss injuries, acts, and consequences of physical abuse and discussed the adequacy of several existing coding systems. The group is continuing to develop an enriched system of definitions and classification of abusive injuries which will serve the purposes of public health, clinical care, social service, mental health, and forensic medical work. Such a system should facilitate communication among physicians, researchers, clinicians, forensic specialists, court officials, and other affected professional disciplines. The group also identified major research questions that need to be addressed to more adequately describe abusive injuries and their consequences. Meeting participants are continuing follow-up activities focused on more adequately describing abusive physical injuries, acts and consequences.

Develop a web site of resources on current reliable and valid tools for measuring and coding injuries, acts and injury consequences associated with child physical abuse. There should be particular attention to resources that assess the mental health consequences of physical abuse including post-traumatic stress disorder (PTSD) and neuropsychiatric problems. The web site should also present resources on child physical abuse from the research literature and resources developed by government sources (e.g. SAMSHA, ACYF, Children's Bureau). The web site should target a variety of audiences such as: physicians, researchers, clinicians, forensic specialists, court officials, social workers and other affected professional disciplines based on market research and evaluation that will inform how to tailor the content to each audience; the web site should be innovative in its use of appropriate web technology (e.g., creative/appropriate use of interactive forms, multimedia) as an educational tool. The user should be able to quickly identify a tool with references for their purpose. The web site should facilitate communication among physicians, researchers, clinicians, forensic specialists, court officials, and other affected professional disciplines on systems of definitions and classification of abusive injuries and their consequences. It should inform public health, clinical care, social service, mental health, and forensic medical work.

Maintain the web site with current information and verify related links. A number of other government agencies provide web-based resources on child physical abuse and the required "tools" (CDC, ACYF, Children's Bureau) and this web site would need to have appropriate and accurate links to those sites. Develop marketing strategies to effectively promote and evaluate the web site: monitor and assess its usefulness (level of interest, knowledge level); usability (navigation, format); and dissemination among intended audiences. A multi-disciplinary approach to this contract is encouraged. Potential contractors should be able to work with experts in the fields of pediatrics, neurology, mental health and allied health care (social psychology, behavioral science, educational psychology, managed care providers), as well as government agencies (Department of Health and Human Services)

and industry (computer technology, social marketing).

038 Developing Test Batteries to Assess Subtle HIV Associated Neuropsychologic Impairment

The purpose of this SBIR contract is to support the development of neurocognitive test batteries in HIV infection. Neuropsychological impairments (NP) and central nervous system involvement are observed in a significant proportion of HIV infected individuals. A severe neurologic complication of AIDS is an HIV associated dementia (HAD) that is characterized by marked cognitive decline, motor dysfunction and behavioral disorders. More common than the severe deficits of frank dementia are the subtle cognitive deficits referred to as mild cognitive disorder or Minor Cognitive /Motor Disorder (MCMD). Different neuropsychological test batteries are required for HAD and MCMD.

It is unclear if there is an increased risk of subtle NP impairment in the early asymptomatic or mildly symptomatic stages (MCMD) of HIV infection. It is likely that subtle NP impairments in asymptomatic individuals could impact on daily living activities of HIV infected asymptomatic individuals. In addition, patients with advanced disease are demonstrating improvements in NP impairments subsequent to HAART therapy. However, it is unclear if patients that are responsive to HAART still retain any subtle neuropsychological deficits.

A range of neuropsychological assessment batteries are currently in use to gauge the degree of HIV induced behavioral dysfunction. However there is a need to develop additional batteries that will assess a wide range of subtle changes in infected individuals in the early stages of disease or those demonstrating improvements in neuropsychological function after therapy. NIMH will support the development of novel neuropsychological test batteries that will detect subtle impairments which could impact on the patients daily living activities. Neurocognitive assessment strategies are critically needed as readily accessible indices for correlative studies of neuroimaging changes of HIV infection.

NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE (NINDS)

The mission of the National Institute of Neurological Disorders and Stroke (NINDS) is to:

- Conduct, foster, coordinate, and guide research on the causes, prevention, diagnosis, and treatment of neurological disorders and stroke, and supports basic research in related scientific areas.
- Provide grants-in-aid to public and private institutions and individuals in fields related to its areas of interest, including research project, program project, and research center grants.
- Operate a program of contracts for the funding of research and research support efforts in selected areas of institute need.
- Provide individual and institutional fellowships to increase scientific expertise in neurological fields.
- Conduct a diversified program of intramural and collaborative research in its own laboratories, branches, and clinics.
- Collect and disseminate research information related to neurological disorders.

This Solicitation invites proposals in the following area:

038 Development of Pain Model Systems and Assessment Tools
(accepting Fast Track proposals)

Millions of patients experience inadequately controlled pain after surgery or trauma. Many more individuals have chronic pain that is poorly controlled or whose treatment causes unacceptable side effects. The cost to individuals includes: suffering, reduced quality of life, lost wages and extraordinary medical expenses. New, more accurate, experimental models and tools for objectively evaluating pain conditions are clearly needed. Tools are needed to elucidate potential analgesic targets, and models for testing and validating these for efficacy in patients. Elements in this effort would be development of quantitative sensory testing for pain patients, surrogate models for pain in volunteers and new clinical outcome measures. Development of new diagnostic tools for

different pain mechanisms and objective measures of analgesic drug action, including functional imaging, would also be extremely valuable as well as ways to monitor pain or pain-related behavior in children.

NINDS is seeking proposals for the development of innovative model systems to study pain and the tools to objectively evaluate the experience of pain.

CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)

NATIONAL CENTER FOR CHRONIC DISEASE PREVENTION AND HEALTH PROMOTION, CENTERS FOR DISEASE CONTROL AND PREVENTION (NCCDPHP)

The NCCDPHP plans, directs, and coordinates programs in health promotion, chronic disease prevention, and reproductive health to enhance quality of life, improve reproductive health, and reduce the incidence of heart disease, stroke, cancer, diabetes, arthritis, obesity, oral disease, infant and maternal morbidity and mortality, unintended pregnancy, and emerging chronic diseases. NCCDPHP uses two essential criteria to prioritize its research portfolio, societal burden and disproportionate burden. NCCDPHP places high priority on chronic diseases and conditions and reproductive health outcomes that have the greatest total impact on health, longevity, and quality of life. NCCDPHP places high priority on eliminating disproportionate burden related to sex, age, race, ethnicity, geography, sexual orientation, socioeconomic status, disability, and special needs. NCCDPHP supports three primary types of applied research, research on cause (determinant research), research on effect (intervention research), and research on application and benefit (dissemination research). NCCDPHP emphasizes cross-cutting research that is participatory, accounts for social and ecological factors, and is implemented at multiple levels.

NCCDPHP has identified ten priority research areas: 1) develop new measures and research designs to strengthen the quality of research; 2) identify the underlying determinants of racial and ethnic health disparities; 3) develop and evaluate interventions to eliminate health disparities; 4) examine established and emerging risk factors for chronic disease and investigate their potential for public health interventions; 5) assess the effectiveness of policy and environmental interventions to promote health; 6) improve the processes and outcomes of health care systems; 7) develop effective communication strategies to promote health; 8) examine methods for helping people manage their own health; 9) develop and evaluate the effectiveness of population-based health promotion and disease prevention policies and programs at local, state, national, and international levels; 10) examine approaches for effectively translating successful community interventions into widespread practice. For examples of specific research questions in each of the ten priority areas, see Setting the Agenda: CDC Research in Chronic Disease Prevention and Health Promotion, available at http://www.cdc.gov/nccdphp/agenda/index.

This Solicitation invites proposals in the following areas:

004 Family-Based Detection of Hereditary Hemochromatosis

Proposals are invited for the development of a model protocol for family-based detection of hemochromatosis. The protocol should include strategies to enable clinicians to identify potentially affected relatives, offer sufficient counseling to allow an informed decision about screening, and ensure follow-up when screening is done. These strategies must protect the privacy and confidentiality of all family members, and must take into account barriers such as the geographic dispersion of family members and multiple different health care payers.

005 Developing a Plan to Promote 5 A Day in New Channels

Proposals are invited for the development of a model protocol for implementing a plan to raise industry and consumer awareness of the importance of 5 A Day through innovative channels, including restaurants. The protocol should be a research based document which includes strategies to enable food producers, growers, restaurant managers, chefs etc. to become knowledgeable of the importance of 5 A Day to their clientele and identify resources that can be used to promote 5 A Day in phases of food service such as menu development, commodity procurement, meal preparation and delivery. The protocol should include best

practices for increasing fruit and vegetable consumption and sales, address barriers for increasing fruits and vegetables on menus and recommendations on how to motivate the commercial food service industry to become interested in promoting the 5 A Day message.

006 Developing an instrument to monitor Pedestrian Activity

Proposals are invited for the development of a mechanical/electrical device that can accurately and unobtrusively quantify walking behavior in a variety of contexts such as parks, trails and sidewalks. The same device may have utility inside buildings such as workplaces or schools. Research and development is needed on how best to address the problems inherent in measuring walking behavior in real world setting. Some of the problems are that people walk in groups as well as on their own, people vary in height and walk at different speeds, and minimization of 'noise' from non–walking behaviors such as cycling or animals. The device would need to stand up to weather conditions and potential vandalism and would ideally require minimal set up equipment or processes. Easy access to stored data is essential.

007 Arthritis and Other Rheumatic Conditions (Self Management, Exercise Equipment Evaluation, Physician and Other Health Care Provider Education/Training)

The Arthritis Program in the Division of Adult and Community Health is working to implement the *National Arthritis Action Plan-A Public Health Strategy* to decrease the burden of arthritis in the United States. Arthritis is the leading cause of chronic pain and disability in the United States. Opportunities exist to reduce the burden of arthritis and its impact by increasing knowledge of arthritis, self management of arthritis, and the importance of physical activity and weight control among both people with arthritis and health care providers.

A. Self Management Programs and Materials

There is interest in the development, application and evaluation of innovative interventions to increase self management, including weight control and physical activity, among persons with arthritis. Self management (weight control and exercise) programs have been shown to have beneficial effects for people with arthritis. Although effective strategies for self management exist, few have been adequately implemented. The focus of proposed projects should reflect target populations at high risk of arthritis.

1. Design, develop, and evaluate a CD-ROM or Web-based arthritis self management programs for different population groups that may include low income, minority, elderly, rural, or non-English-speaking audiences.
2. Design, develop, and evaluate education materials (e.g., videos, cassettes, workbooks, etc.) addressing self management for different population groups that may include low income, minority, elderly, rural, or non-English-speaking audiences.
3. Design, develop and evaluate weight control (weight loss) programs and/or materials that are safe and effective for people with arthritis.

B. Exercise equipment and assistive devices

There is interest in the development, application and evaluation of exercise equipment appropriate for people with arthritis and other rheumatic conditions. Persons with arthritis need to do both aerobic and resistive physical activity. There is limited amount of exercise equipment that is safe and easy to operate by persons with arthritis who are unable to use existing exercise equipment.

1. Design, develop and evaluate low-impact exercise equipment designed to be safe and easy to operate by people with arthritis and other rheumatic conditions who are unable to use existing exercise equipment.
2. Design, develop and evaluate resistive exercise equipment designed to be safe and easy to operate by people with arthritis and other rheumatic conditions who are unable to use existing exercise equipment.
3. Develop adaptive equipment, assistive devices, and/or instructional materials directed toward preventing or minimizing functional limitations or preserving independence among

persons with arthritis and other rheumatic conditions.

C. Physician and Other Health care Provider Education/Training

Methods are needed to increase awareness of self management and develop programs to build self management education and physical activity recommendations into routine care for people with arthritis and other rheumatic conditions.

1. Design, develop and evaluate materials to educate or train physicians and/or other health care professionals on the importance of self management and how to foster increased self management among their patients.

2. Design, develop and evaluate materials to educate or train physicians and/or other health care professionals on the importance of physical activity and how to foster increased appropriate physical activity among their patients.

008 Development and Evaluation of Innovative Community Approaches for Self-Management Training

As reviewed recently (see Norris et al., Diabetes Care 2001;24:261-87), evidence supports the short-term effectiveness of self-management training in type 2 diabetes, but research is needed to assess the long-term effectiveness of such interventions on glycemic control, development of microvascular and macrovascular disease, and quality of life, especially for self-management training conducted in community settings, rather than clinics and other health-care settings. DDT solicits research applications to develop and evaluate 1) optimal methods of delivery of home-based interventions (including but not limited to the roles of family, lay health-care workers such as promotoras, and computer-assisted instruction); and 2) approaches for identifying persons who would benefit from community approaches, maximizing participation and retention, and linking interventions with primary care. DDT encourages research to explore how settings, providers, and specific intervention characteristics (content, duration, frequency) interact to achieve optimal results in diverse populations and settings. Research is also needed to compare barriers and effectiveness of interventions in community settings and clinics, especially for high-risk minority populations. Research to examine the relative costs and prevention effectiveness of different approaches and potential mechanisms for integration within health-care systems will also be considered.

009 Role of Lipoprotein Subfractions in Risk for Complications of Diabetes

As summarized by the American Heart Association, diabetes is a major independent risk factor for cardiovascular complications, including coronary heart disease, stroke, peripheral artery disease, nephropathy, retinopathy, and possibly neuropathy and cardiomyopathy (see Grundy et al., Circulation 1999;100:1134-46). Diabetes causes preventable complications that can be life-threatening, including kidney disease and amputations; the most serious complications are associated with macrovascular and microvascular disease. In addition, cardiovascular disease is the major cause of mortality in persons with diabetes, including women. Recent research findings indicate that ischemic heart disease risk varies, even among normocholesterolemic persons, according to concentrations of various LDL, HDL, and VLDL subfractions. However, because measurement of lipoprotein subfractions is time-consuming, labor intensive, and requires sophisticated instrumentation, these determinations are not widely performed, and few data are available for persons with diabetes. In addition, different research laboratories use different analytical approaches and no reference method or standard reference material is available, so results vary among laboratories and may not be comparable.

Newer analytical methods, including NMR, have shown promise in addressing these limitations.

DDT solicits applications for research to 1) describe lipoprotein subfraction distributions and their associations with other cardiovascular risk factors in persons with diabetes, 2) evaluate the role of lipoprotein subclasses and particle size as risk factors for the development of macrovascular and microvascular complications in persons with diabetes, and 3) determine the impact of improved diabetes care (including better glycemic control, use of hypoglycemic and other medications, and lifestyle interventions) on lipoprotein subclasses. Because of the recent emergence of type 2 diabetes in children and

adolescents, especially in minority populations, research applications to explore lipoprotein subclasses in children and adolescents with diabetes are encouraged. Applications for research to examine lipoprotein subfraction distributions and their correlates in persons at increased metabolic risk for diabetes, including individuals with insulin resistance, impaired fasting glucose, and impaired glucose tolerance, will also be considered.

010 Methodology for Imputing Missing Data in Nationally Representative Surveys

Statistical methods to analyze datasets that have missing data have been available for several years (see Schafer, 1977). These methods are rarely used in public health and epidemiologic research, although missing data are ubiquitous. Research on developing, implementing, and testing new methods for imputing missing data has the potential to improve survey research and to improve public health practice and policy making, which is often based on survey data. DDT is specifically interested in encouraging methods research for imputing income data and race/ethnicity data, which are often missing in large population-based surveys such as the Behavioral Risk Factor Surveillance System (BRFSS) and the National Inpatient Sample (NIS), respectively.

Schafer JL. Analysis of Incomplete Multivariate Data. London: Chapman & Hall, 1977.

011 Validation of Measuring Diabetes Preventive Care Practices

Diabetes-related preventive care practices (e.g., self-care and physician practices such as annual foot and eye exams, hemoglobin A1c testing, and diabetes self-management education) have the potential to prevent or delay the development of complications from diabetes. Because of the critical importance of preventive care practices, diabetes surveillance systems and initiatives to improve quality of diabetes-related care monitor trends in preventive care practices. The validity (e.g., sensitivity, specificity, predictive value positive) and reliability of methods using interview data, administrative data, and medical records to measure the delivery or receipt of preventive care practices have not been well characterized. However, some studies have suggested that the specificity of preventive care practices is not high, their sensitivity depends on the measure or indicator, and that medical record review is an imperfect gold standard for assessing validity. A greater understanding is needed of the validity and reliability issues surrounding the measurement of preventive care practices for persons with diabetes. DDT encourages research to characterize and summarize these measurement issues and to develop, compare, and evaluate new approaches to improve measurement of preventive care practices, including comparison of the sensitivity, specificity, predictive value positive, and reliability of general and diabetes-related preventive care practices.

012 Examine Approaches for Effectively Translating Successful Community Interventions Into Widespread Practice

Tobacco Prevention and Control Knowledge Management System

Tobacco use is the single most preventable cause of death and disease in our society. Annually, tobacco use causes more than 430,000 deaths and costs the Nation $50-73 billion in medical expenses alone. However, a great deal is known about how to prevent tobacco use and promote quitting among people who already use tobacco. This information is contained in a variety of formats, including the Surgeon General's report on *Reducing Tobacco Use*, CDC's *Best Practices for Comprehensive Tobacco Control Programs*, the Task Force on Community Preventive Services' tobacco-related recommendations, the Public Health Service guidelines on smoking cessation and various research and evaluation reports and publications. It is clear that there is considerable knowledge that is not being used, and that new knowledge is continually emerging.

Proposals are being invited for the development of a web-based, interactive tobacco prevention and control knowledge management system, capable of yielding the following types of information: 1) methods of health promotion and disease prevention tactics and strategies, classified by varying levels of effectiveness, given demographic and contextual indicators, 2) the health effects likely to result from effective applications of these tactics and strategies, 3) the cost of those tactics and strategies and their potential non-health impacts, 4) health and social policy implications, and 5) research gaps and needs.

The system should be designed such that users could augment the system based on their own experience and research, given appropriate protocols and quality assurance standards. In addition, consideration should be given to the ability of the system to incorporate other non-tobacco risk factors for chronic disease prevention and control.

013 High through-put method to isolate tobacco and tobacco-derived cigarette components

The Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, in collaboration with the National Center for Environmental Health (NCEH) are working to collect, analyze, and disseminate data relating to the effect of cigarette smoking on human health and to develop methods for improved information related to smoking and health. Part of this effort involves the laboratory analysis of cigarettes by the Air Toxicants Branch, NCEH.

The combustible column of a cigarette is composed of a variety of tobaccos, additives, and paper. The American-type blended cigarette typically contains 4 types of tobacco - Virginia, Burley, Maryland, and Oriental in the form of tobacco leaf (lamina), cut rolled stems, expanded tobacco, and paper and bandcast reconstituted tobacco sheet. The chemical composition of these tobaccos varies, such that levels of nicotine and tar in cigarette smoke are influenced by their relative proportions in a cigarette (Browne 1990). Further, the nicotine content of a tobacco product can be increased with nicotine-fortified reconstituted sheet (Silberstein 1985).

Understanding the design and construction of cigarettes is integral to research into the health consequences of smoking. Changes in product composition or design (e.g., the presence or absence of an additive, tobacco cut-width, smoke pH, degree of ventilation) can influence the toxicity of cigarette smoke. Consequently, it is necessary to separate cigarette components (e.g., reconstituted sheet) in order to determine their chemical composition and evaluate their contribution to levels of nicotine and other toxic chemicals in smoke. Separating the cigarette filler components by hand with magnification is difficult and time-consuming, hampering efforts to obtain sufficient material for research purposes.

Isolate tobacco and tobacco-derived cigarette components. Proposals are invited for the development of a method (i.e., method, technique, instrument, or device) to separate cigarette filler consisting of tobacco and tobacco-derived components (i.e., bright, burley, and Oriental tobacco, stems, puffed tobacco, paper reconstituted tobacco, and bandcast reconstituted tobacco). The method should also be applicable to other combustible tobacco products such as bidis, clove cigarettes, and cigars. The method should be of sufficiently high through-put to allow practical quantities of tobacco and tobacco-derived components to be separated in less than 24 hours. An example of a practical quantity is the amount of tobacco and tobacco-derived materials contained in a pack (i.e., 20 cigarettes) of cigarettes. Each separated fraction should contain less than 5% carry-over of other materials.

References:

Browne CL. 1990. *The Design of Cigarettes*. Third edition. Hoechst Celanese. pp. 1-118.

Silberstein DA. 1985. Flavouring reconstituted tobacco. Tobacco Journal International 1:26-29.

014 Method to screen tobacco products for reduced-harm or reduced-exposure claims

The Centers for Disease Control and Prevention (CDC) is engaged in activities to collect, analyze, and disseminate data relating to the effect of cigarette smoking on human health and to develop methods for improved information related to smoking and health. Part of this effort involves the biomonitoring research conducted by the Air Toxicants Branch, National Center for Environmental Health, CDC. Biomonitoring research attempts to identify and measure markers of chemical exposure (e.g., exposure to cigarette smoke or environmental tobacco smoke (ETS)) and also biochemical, physiologic or other alterations that represent, or serve as a proxy for, an established or potential harmful effect produced by a chemical exposure.

The traditional American-style cigarette contains a combustible column composed of a variety of tobaccos, additives, and paper. The tobaccos and tobacco-derived materials can consist of Virginia, Burley, Maryland, and Oriental in the form of tobacco leaf (lamina), cut rolled stems, expanded tobacco, and paper and bandcast

reconstituted tobacco sheet. The chemical composition of these tobaccos varies, such that levels of nicotine and tar in cigarette smoke are influenced by their relative proportions in a cigarette (Browne 1990). Cigarette smoking is a cause of coronary heart disease, atherosclerotic peripheral vascular disease, cerebrovascular disease, cancers of the lung, larynx, mouth, esophagus, and bladder, chronic obstructive pulmonary disease, intrauterine growth retardation, and low-birth weight babies (PHS 1989, 1990).

Since the late 1980's, cigarette manufacturers have begun to market and sell "reduced-exposure" products. For example, in 1988 the R.J. Reynolds Tobacco Company introduced the Premiere cigarette. The premise behind the new cigarette technology was a decrease in the complexity of the smoke chemistry, reduced second-hand smoke, and lower rates of toxicity in a battery of tests. Premiere was not accepted by smokers and was taken off the market after several months (Eclipse Expert Panel 2000).

In 1996, RJR began to test market the Eclipse cigarette. Similar to its predecessor Premiere, Eclipse primarily heats tobacco. One difference between the two products is that the Eclipse cigarette also burns a small amount of tobacco (Borgerding et al. 1997).

In advertising and mass mailings, RJR promotes Eclipse as a cigarette that "may present less risk of certain smoking-related diseases." This claim is based on lower levels of toxic chemicals in the smoke, fewer tumors in animal studies, and fewer health effects in people who smoke Eclipse (i.e., bronchial inflammation, levels of mutagens in urine, inflammatory cell counts) than traditional cigarettes. RJR further states, "The best choice for smokers who worry about their health is to quit. But for those who choose to smoke, the next best choice is Eclipse."

In order to improve consumer acceptance, RJR has developed several Eclipse prototypes (Eclipse Expert Panel 2000). The overall affect of these product modifications on levels of harmful chemicals in the smoke and toxicity of the product have not been made public by the company.

Introduction of products such as Eclipse with the promise of reduced exposure and reduced harm may increase initiation and increase, decrease, or have no effect on quit attempts (Institute of Medicine 2001). It is also conceivable that these products may increase relapses among former smokers that would smoke again if the health risks of cigarettes were perceived as being eliminated. To design successful public health programs that address new and emerging tobacco product technologies such as Eclipse, Accord, and Advance, information is needed on how these products compare to traditional cigarettes with respect to toxicity and smoke chemistry. Stated claims of lower yields of specific chemicals need to be verified under conditions relevant to how the product is smoked by people, not only by the Federal Trade Commission method with an automated smoking machines (NCI 1996). Technologies such as those used in a self-extinguishing cigarette need to be monitored for an overall increase in the harmfulness of the product. A research tool is needed that allows researchers to quickly evaluate and react to tobacco product claims and new technologies. An example is the multi-gene array technology that is under consideration for detecting and categorizing changes in gene expression caused by environmental chemicals (Miller 2001; Rosen and Chernoff 1999).

To Aid in Monitoring health and exposure claims for new and emerging tobacco product technologies. Proposals are invited for the development of the technology that will lead to a method (i.e., method, technique, instrument, or device) or methods to rapidly, yet accurately, monitor reduced-harm and reduced-exposure tobacco product claims. The method should address claims of lowered levels of specific chemicals in the smoke (e.g., nicotine or tobacco-specific nitrosamines) of tobacco products. The method should also employ technology to evaluate made or implied reduced-harm claims (e.g., respiratory tract toxicity and cancer). The method should be applicable to a wide variety of tobacco products including self-extinguishing cigarettes (e.g., Merit, manufactured by Philip Morris), modified emission (i.e., "reduced-exposure") products (e.g., Advance, manufactured by Star Scientific and Accord, manufactured by Philip Morris), and products that employ novel technologies such as R.J. Reynolds' Eclipse, a nicotine delivery device that heats, rather than burns tobacco. The method must allow comparisons with traditional cigarettes (e.g., Marlboro Lights, Winston, and Newport) or experimental reference cigarettes (e.g., Kentucky reference cigarettes). When fully developed, the method

should be of sufficiently high through-put to allow a practical number of brands to be investigated and results to be generated in a reasonable length of time. At least 5 brands are considered a practical number of brands. A reasonable length of time is considered 3 to 6 months to perform such tests.

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NATIONAL CENTER FOR INFECTIOUS DISEASES (NCID)

The NCID plans, directs, and coordinates a national program to improve the identification, investigation, diagnosis, prevention, and control of infectious diseases. In carrying out this mission, the Center: (1) Provides leadership in investigation and diagnosis of infectious diseases of public health significance including emerging and reemerging infections; (2) maintains surveillance of infectious diseases, disability, and death; (3) conducts applied and operational research related to definition, distribution, diagnosis, prevention, and control of infectious diseases, including vaccine development; (4) administers a biological reagents program which includes research on production; development of guidelines for production and utilization; and standardization, production, and distribution of reference reagents; (5) produces, evaluates, and distributes experimental vaccines, antisera and antitoxins, skin test antigens, and immune serum globulins to control and prevent laboratory infections and to prevent or minimize illness in certain population groups; (6) produces and distributes microbiological reference and working reagents not commercially available or of unreliable supply; (7) conducts applied research related to vectors of disease; (8) provides epidemic assistance; (9) maintains competence in the detection, identification, and control of rare, exotic, or tropical diseases; (10) provides reference diagnostic services; (11) provides technical assistance to States and localities and to other nations in the investigation, diagnosis, prevention, and control of infectious diseases; (12) provides scientific services in support of CDC's laboratories; (13) in carrying out the above functions, collaborates, as appropriate, with other Centers and Offices of the CDC.

This Solicitation invites proposals in the following areas:

029 Development of Innovative Host-Targeted, Systemic Flea Control Products that Contain Insect Growth Regulators

Fleas are the primary vectors of plague and murine typhus. These insects also have been implicated recently as vectors of *Bartonella henselae,* the causative agent of cat scratch disease. At present, the most commonly

recommended means for reducing human risk of flea-borne diseases is through application of insecticidal dusts to rodent nests, burrows and runways, or by treating animals with these same agents when they visit bait stations. Although such approaches have generally proven effective, the application of traditional insecticides can pose problems. This is especially true when local residents express concerns about the potential or perceived adverse environmental effects of these insecticides on their families, pets, and other non-target organisms. The use of insect growth regulators represents an alternative approach to flea control that might be both effective and more environmentally acceptable. These agents are reported to be highly specific for arthropods and virtually harmless to non-target organisms.

Proposals are invited for the development of innovative host-targeted, systemic flea control products that contain insect growth regulators and can be administered as 1) oral baits in bait stations, or 2) through the broadcasting of baits in rodent habitats. Proposals should include the following:

A. A detailed plan identifying how vector fleas can be controlled through the use of oral baits containing an insect growth regulator(s) selected by the contractor. The proposal also should provide a written justification (supported by references from the scientific literature) describing why certain insect growth regulators were selected for development of the requested baits.

B. The contractor should describe and conduct a pilot study to assess the efficacy of these baits and the feasibility of the selected delivery method. The pilot study should include *in vivo* laboratory trials of the bait formulations in each of the rodent hosts mentioned in item 4.

C. The proposal should outline methods for maintaining breeding colonies of disease-free fleas. It is requested that *Xenopsylla cheopis* fleas, which are vectors of plague and murine typhus, be included in the study, although trials with other rodent fleas are strongly encouraged.

D. Because persons working with wild-caught rodents are likely to be at greater risk of infection with zoonotic pathogens than other individuals who work with laboratory-reared colonies of the same species, it is requested that the contractor outline a plan for 1) the safe capture and handling of wild rodents and 2) the subsequent establishment of breeding colonies of disease-free rodents. The rodents requested for these colonies are *Rattus norvegicus*, *Spermophilus variegatus, Spermophilus lateralis* and *Neotoma albigula*, which are known hosts of plague, murine typhus or *Bartonella*. The contractor also should supply sufficient numbers of these animals and the oral bait product to allow for independent testing by CDC personnel.

030 Detecting West Nile Virus and Other Arboviruses of Public Health Importance in Mosquito and Non-Human Vertebrate Samples Used in Surveillance Programs

There is a need for the development of rapid, qualitative, and economical techniques for detecting West Nile virus and other arboviruses of public health importance in mosquito and non-human vertebrate samples used in surveillance programs. Methods may be based on viral antigen detection by antigen capture enzyme immunoassay or fluorescent antibody staining, on viral RNA detection, or other appropriate technology. Methods must be of sufficient sensitivity to be of use in predictive surveillance programs. Also, methods should be able to identify and separate the primary arboviruses of public health importance in the United States (West Nile virus, St. Louis Encephalitis virus, eastern equine encephalitis virus, western equine encephalitis virus, and La Crosse virus). Methods should be developed to eliminate or reduce the need for expensive, specialized equipment; to include in kit form all of the necessary reagents and supplies; to incorporate internal quality controls; and to reduce or eliminate risk of operator infection with infectious agents. Such methods would be valuable in making arbovirus surveillance possible in areas not supported by comprehensive diagnostic or research laboratories, in permitting rapid processing of important surveillance samples in emergency situations, or in other situations where very rapid turnaround is desirable.

NATIONAL CENTER FOR INJURY PREVENTION AND CONTROL (NCIPC)

The National Center for Injury Prevention and Control plans, directs, and coordinates a national program to maintain and improve the health of the American people by preventing premature death and disability and reducing human suffering and medical costs caused by nonoccupational injury, addressing both intentional injuries that result from violent and abusive behavior and unintentional injuries. The national program encompasses the prevention of nonoccupational injuries, and applied research and evaluations in acute care and rehabilitation of injured persons. The Center will address injury prevention and control through an orderly sequence of activities beginning with research on causes, circumstances, and risk factors; progressing through research on interventions and their impact on defined populations. These activities then lead to the broad, systematic applications of interventions that are soundly based scientifically.

CDC is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2010", a PHS-led national activity for setting priority areas. CDC encourages applicants to submit grant applications with relevance to the specific objectives of this initiative. Potential applicants may obtain a copy of "Healthy People 2010"; (Full Report: Stock No. 017-001-00537-1): through Superintendent of Documents, Government Printing Office, Washington, D.C. 20402-9325 Telephone (202) 512-1800.

This Solicitation invites proposals in the following areas:

001 Reducing the Lethality of Acetaminophen Poisonings through Formulation with Methionine

Acetaminophen poisonings, both intentional and unintentional, are common in this country. A cursory look at a national sample of recent emergency department records suggests it may be the most commonly used drug used in overdoses. The resultant effects on the liver can be eventually fatal. The toxicity of the drug can be dramatically reduced, however, if it is formulated in combination with methionine, an amino acid. This formulation has been suggested in British literature as a way to prevent these deaths. Yet no drug company is making this combination. If this combination eventually is accepted as a substitute for acetaminophen, the demand for it would be tremendous. The net effect would be a benefit for suicidal individuals as well as toddlers who ingest acetaminophen, an over the counter drug that is available in almost all homes.

Proposals are solicited for the research, development, and commercialization of a nontoxic formulation of acetaminophen to reduce the number of poisonings due to this drug.

002 Reducing the lethality of Overdoses through Formulation with Two-Part Emetics

Vomiting-inducing agents (emetics) formulated in combination with drugs used in overdoses have been suggested previously as a way to counteract overdoses, intentional and otherwise. The problem is that the effects of such emetics may be felt when the drug is taken as directed. This proposal attempts to fund a search for two-part emetics that produce vomiting when taken in combination. Compound A could be an emetic that is activated by a catalyst, compound B. Compound A alone would be added to half of the capsules of a given drug that is frequently used in overdoses. A little of compound B alone would be added to the other half that lack compound A. The user would not know which has A and which has B. Taking one pill at a time (as directed) will never induce vomiting. Taking a handful of pills intentionally or unintentionally, in contrast, will in a very high percentage of incidents involve ingestion of both A and B and subsequent vomiting, thus mitigating the effects of overdoses.

This approach would of course require that health care providers not prescribe taking two pills on each occasion, but this should not be a terrible burden on providers, especially if two-part emetics are used only in those drugs currently favored by suicidal individuals.

Proposals are solicited for the research, development, and commercialization of emetics formulated in combination with drugs used in overdoses to reduce the incidence of intentional and unintentional poisonings.

003 Carbon Monoxide Detectors in the Passenger Compartments of Automobiles

Technology exists to create miniature carbon monoxide detectors that can be exposed to the air of the passenger compartment of automobiles and multi-passenger vehicles. Such detectors can be programmed to signal a warning when CO levels become unhealthy and then to turn off the engine if the levels do not drop within a prescribed interval. The purpose of such devices is the prevention of some of the 1200 CO suicides annually and some of the 300 unintentional CO deaths annually in the United States. Prototypes of these devices do not exist for automobiles, but they have been designed for industrial settings where their purpose is to turn on ventilation fans when air CO levels become harmful. SIBR funding could be used to apply the technology to create an automobile prototype. This process would allow better estimation of the unit cost of the devices and would inform the kinds of cost-benefit analysis that regulatory agencies would probably require before mandating such devices on new vehicles. Prospects for such devices being recommended by cost-benefit analysis are good given that experts estimate they can be produced for $12 apiece. There are more expensive safety devices in automobiles that have been estimated to save fewer lives than those lost annually to automotive CO poisoning.

Proposals are solicited for the research, development, and commercialization of a carbon monoxide detector that would sound an alarm and shut off a vehicle's fossil fuel powered engine. The purpose of such devices is the prevention of some of the 1200 CO suicides annually and some of the 300 unintentional CO deaths annually in the United States.

NATIONAL CENTER FOR HIV, STD AND TB PREVENTION (NCHSTP)

The Division of STD Prevention provides national leadership through research, policy development, and support of effective series to prevent sexually transmitted diseases (including HIV infection) and their complications such as enhanced HIV transmission, infertility, adverse outcomes of pregnancy, and reproductive tract cancer. We assist health departments, health-care providers, and non-governmental organizations and collaborate with other governmental entities through the development, synthesis, translation, and dissemination of timely, science-based information; the development of national goals and science-based policy; and the development and support of science-based programs that meet the needs of communities.

This Solicitation invites proposals in the following areas:

005 CD-ROM for Patient Counseling

Develop an interactive CD-ROM to (1) obtain in-depth sexual histories from patients, and (2) deliver, enhance, and reinforce STD prevention counseling. The CD-ROM would supplement current, standard-of-care history-taking and counseling practices in clinical settings serving adolescent patients, such as public health clinics, STD clinics, and private practice settings. The sexual history component ill present questions in a manner that takes into account the sensitivity of the topic. The counseling component will be responsive and tailored to each patient's developmental level, demographic profile, and readiness for behavior change.

The objectives of the CD-ROM would be to (1) obtain sexual history information via audio-enhanced computer-assisted self-interview (audio-CASI), (2) provide individually- tailored sexual risk reduction messages (e.g., the importance of condom use, instruction in correct condom use); (3) evaluate patients' comprehension of knowledge gains through corrective feedback; (4) provide tailored messages to promote internalization of prevention messages (e.g., assessment of barriers to condom use, perceived norms regarding condom use).

006 "Can You Adequately Assess Your Clients' HIV/STD Risk?"

Develop a video designed to train health care providers (e.g., physicians, nurses, disease intervention specialists) to conduct a thorough, appropriate HIV/STD risk assessment during a standard office visit. This 20-30 minute video would target health care providers in both the public and private sectors. The video would focus both on what constitutes an HIV/STD risk assessment (e.g., sexual history, drug use, STD history) and the communication skills providers need to effectively interact with their clients

during the assessment. Innovative instructional methods as well as skits designed to demonstrate sensitive/insensitive techniques should be included. The video could be marketed toward public clinics such as STD, HIV, and family planning clinic staff, and private sector health care providers including large managed care organizations.

007 Develop a Video Targeting Teen Girls and Young Adult Women Thinking about Reducing Sexually Transmitted Disease in Pregnancy

Based on a recent three-site study by CDC (Greenberg et al., 2000. *Evaluation and the Health Professions*, 23:123-148), a considerable number of women at high risk for sexually transmitted diseases (STDs), including HIV infection, may be trying to become pregnant.

Develop a video targeting STD risk in pregnancy that would supplement current intervention efforts in settings that serve women engaging in high-risk sexual behavior. This 15-25 minute video would address teen girls and young adult women who are at risk for STDs and who intend to become pregnant. The focus would encourage women to think about reducing risks of STD infection during pregnancy through prior couples' testing for HIV, syphilis, and other STDs that may effect the fetus as well as safer sex practices during pregnancy. The video would be suitable for venues such as family planning clinics and STD clinics. Ideally it would be viewed prior to the patient's physical examination to stimulate discussion between medical providers and female clients on STDs and pregnancy.

008 "Factorial Survey Tool for Gathering Detailed Data"

Factorial survey research techniques have the potential to be useful across the spectrum of public health research, but the field lacks useful and widely available software with which to construct them.

Developing software for a survey tool. The logic model for factorial survey construction is such that there exists (a) *x* number of variables, with (b) *y* levels of each variable, and (c) some response scale. There is a need for the development of a software program encompassing this logic model with four essential goals. First, the format must enable the user to construct a variable number of items with variable levels within each item, and a response scale. Second, the program must permit all of (a) random distribution of items and/or levels, and (b) a user-defined pattern of items and/or levels. Third, the program must either have a complete statistical analysis program attached or be compatible with commonly used existing software (e.g., SAS, SPSS). Fourth, the software must be at least sufficiently user-friendly such that a public health professional with access to guides and/or manuals can construct a useful survey.

The software must meet four goals. First, the survey developers must be able to use the software accurately. Second, survey administrators must be able to disseminate the survey accurately. Third, respondents must provide data with at least as few missing responses and at least as high a response rate as with traditional surveys. Fourth, resulting data must be at least as objectively useful to public health professionals (research and program) as data gathered via traditional methods.

009 Syphilis Risk Awareness and Reduction Video

Given the current effort to eliminate syphilis in the US, it would be advantageous to develop educational materials that target syphilis prevention and treatment as well as the broader impact that syphilis prevention has on the incidence of HIV.

Develop a risk awareness and reduction video that illustrates syphilis risk identification, transmission, symptoms, screening, treatment, partner services, behavioral risk reduction change, maintenance and the role of syphilis in HIV transmission. The video would primarily target people who utilize health care settings where they could obtain screening and treatment for syphilis, HIV and other sexually transmitted diseases. However, the video can also be used in settings where counseling and referrals for syphilis testing can be offered. The video will include factual information, storytelling and accounts of personal risk experiences to illustrate the impact that syphilis infection and its prevention on HIV incidence, patients, partners, relationships, and communities.

010 Rapid Assessment of STD Prevention and Treatment Curriculum for Health Educators

Existing training manuals and curricula for rapid ethnographic assessment often recommend consultation with an experienced ethnographer at some time during the process.

Develop a curriculum for use by health educators at local health departments, clinics, community based organizations, and other agencies or organizations that deliver STD prevention and treatment services. The curriculum will target small scale rapid assessment of STD prevention and treatment needs and provide sufficient content to eliminate the necessity of consultation with an expert in ethnographic methods. Content will include definition of problem and target population, data collection and analysis methods, and presentation strategies. The curriculum will define goals and measurable objectives. Elements or activities will be linked to the methodological framework.

011 Adolescent STD Media Campaign

Develop a media campaign targeting adolescents that would inform/encourage them about the need to get tested for sexually transmitted diseases, where to go for testing, and address the issues of confidentiality of results and treatment. The campaign should include television, radio and billboard and Internet media. Campaign messages should be developed by a team of adolescents, ages 13-19, and use appropriate language and images. The campaign should provide a hotline telephone number for adolescents to call to be referred to a nearby provider or clinic where they could be tested and treated, if necessary.

012 Training and Health Communications

A. Develop and evaluate the effectiveness of a video for physicians that will: (a) increase their index of suspicion for syphilis, (b) motivate them to support the National Plan to Eliminate Syphilis from the United States, (c) educate them about the need to quickly report positive syphilis test results to the health department, and (d) educate them about counseling issues related to syphilis. Educating public and private physicians in areas with high syphilis morbidity (HMAs - high morbidity areas) is important to accomplish the goals and objectives of the National Plan to Eliminate Syphilis from the United States. A nationwide survey of primary care physicians found them to be lacking in STD test reporting and counseling knowledge. Additionally, because syphilis is at very low rates, many primary care physicians do not routinely encounter patients with syphilis and may exclude syphilis in their differential diagnosis. For syphilis elimination to become a reality, public and private physicians must be motivated to appropriately test for syphilis and to promptly report positive test reports to the health department for quick intervention to break the chain of infection.

B. Develop and evaluate the effectiveness of a video targeted to community-based organizations (CBOs) that will motivate them to become partners in STD prevention activities at the local level. The video should include basic information on the most prevalent STDs, why it is important to prevent STDs, highlighting the link between STDs and HIV transmission and acquisition, and examples of “best practice” collaborations between CBOs and governmental agencies.

C. Develop and evaluate the effectiveness of videotapes or other educational materials to help consumers talk to their health care providers about STDs. Materials should be developed for both males and females and should be appropriate for viewing or reading in a clinic or private office waiting room. Since it has long been known that health care providers often to not address sensitive topics, such as STDs, with their patients, this approach seeks to enable the consumer to initiate such a dialogue.

D. Develop a CD-rom, audiotape, videotape, or self-instruction manual that will assist non-Spanish speaking health care providers in obtaining sexual histories and providing STD education/counseling to Spanish-speaking clients.

E. Develop interactive software to update health care providers on current approaches for the diagnosis and treatment of STDs.

NATIONAL CENTER FOR ENVIRONMENTAL HEALTH (NCEH)

The National Center for Environmental Health at CDC works to provide national leadership, through science and service, that promotes health and quality of life by preventing illness, disability and death from interactions between people and their environment. NCEH directs programs to prevent the adverse health effects of exposure to toxic substances and to combat the societal and environmental factors that increase the likelihood of exposure and disease.

NCEH main activities:

- National leadership in prevention programs, global health, and the use of human genetic knowledge, tests, and services
- Public health surveillance
- Applied research
  - Epidemiologic studies
  - Laboratory analyses
  - Statistical analyses
  - Behavioral interventions
  - Operations and systems research
- Communication and education
- Standards, guidelines, and recommendations
- Training and technical assistance of officials of state and local health agencies in preventing and responding to public health challenges

This Solicitation invites proposals in the following areas:

001 Environmental Hazards and Health Effects

A. Noise-Induced Hearing Loss in Children and Young Adults

1. Identification and development of databases for the analysis of noise-induced hearing loss in children and young adults.
2. Development of a surveillance database for noise-induced hearing loss in children and young adults.
3. Development of prevention material for noise-induced hearing loss, including references to the noise produced by common non-occupational exposures.

B. Household Exposures to Hazardous Substances

1. Development of a survey instrument and conduct of a survey for consumer products used in homes that contain hazardous substances.
2. Development of a database to link consumer products, hazardous substances, and toxicologic data.
3. Development of educational materials related to hazardous materials in consumer products found in the home, risks associated with these materials, and prevention strategies.

C. Nutritional Supplements

Development of databases for identifying trends in the type, purchase, and/or use of nutritional supplements.

D. Prevention of Heat-Related Deaths Among the Elderly

1. Develop a practical, inexpensive device to alert elderly persons to potential life-threatening temperature extremes in their dwellings, with information on preventive actions to be taken. (For example, a thermometer-like device with easy to read instructions and information on what action to take when a dangerous indoor temperature is reached.)
2. Test the utility of a practical and inexpensive device by distributing them to a sample of elderly people and measuring its acceptability and use.
3. Develop companion educational materials for radio and TV stations during heat waves.

002 Emergency and Environmental Health Services

A. Geographic Information System (GIS) Based Population Estimation and Sampling Software for Natural Disasters and Complex (Refugee) Emergencies

1. Develop a software “add-on” compatible with major GIS packages,

including ArcView and ArcInfo, which will simplify and streamline a GIS based population estimation method developed by CDC, for use in natural disasters and international complex emergencies. This software will also be able to simplify and guide area-based cluster sampling for public health surveillance.

2. Field test the utility and accuracy of the software by comparing results from other sampling and estimation methods. Outcome indicators should include complexity of use, time, and human resources needed to estimate a population and guide an area based cluster sample.

3. Develop an operations manual to use the software in conjunction with major GIS packages and common data sources.

B. Consolidation of Guidelines and Recommendations Regarding Health and Public Health in Humanitarian Emergencies

1. Produce a computer program containing all important guidelines and recommendations pertaining to health and public health in humanitarian emergencies. This may involve obtaining copyright permission to reproduce this material onto a compact electronic data storage medium, such as CD-ROM.

2. Create software to allow dynamic searches of all materials, manipulation of text, and printing text and graphics.

3. Test the acceptability of this new reference tool among members of the field staff of non-governmental organizations, donor governments, and United Nations agencies.

C. Rapid Extraction Device for Chemical Mass Casualties

1. Develop a simple device for the rapid extraction from the contaminated area (hot zone) of non-ambulatory mass casualties resulting from a chemical weapon release. This device will facilitate the rapid removal of victims from the contaminated area to an area more proximate to the decontamination and treatment zones. It will be attached by rope to winches or other similar mechanisms to pull victims to the decontaminated area. By reducing the time of extraction, victims will receive treatment and decontamination sooner, improving the probability of survival.

2. The device should be inexpensive (EMS units will need multiple devices), easily applied (workers will be wearing cumbersome protective gear), must be free of sharp edges (device should not violate workers' protective suits), and should provide reasonable protection of the victim's head and upper body (they will potentially be dragged over rough terrain).

3. Other requirements include the ability to be used multiple times during the same event, able to be decontaminated after an event, require minimal storage space, and be lightweight. Training in the use of the device should be minimal. Field testing of the device will be necessary to evaluate effectiveness and durability.

003 Environmental Health Laboratory Sciences

A. Coronary Heart Disease

The development of a laboratory technology to standardize and improve the quality and reliability of laboratory tests for cholesterol and other metabolically related lipids and lipoproteins that are known risk factors associated with coronary heart disease is an area in which the SBIR program may be able to contribute to the improvement of diagnostic techniques.

Specifically:

Development and characterization of improved serum reference materials that can be used by NCEH to standardize laboratories which conduct epidemiological and lipid research and clinical trials into the causes and prevention of coronary heart disease.

B. Cystic Fibrosis and Medium Chain Acyl Dehydrogenase Deficiency

The development of DNA-based materials containing the pertinent mutations for the screening of Cystic Fibrosis (CF) and Medium Chain Acyl Dehydrogenase

Deficiency (MCAD) from newborn dried blood spot specimens. The materials should be in the form of blood dried into an FDA-approved filter paper blood collection device. The materials should provide the appropriate DNA sequences that will respond to mutation analysis methods such as DNA amplification by PCR, restriction fragment length polymorphism analysis, and nucleotide sequencing. These materials are needed to help standardize and improve the quality and reliability of laboratory tests that are used to screen for CF and MCAD at birth. Currently, there is no commercial source available for the DNA-based materials for these disorders.

C. Tests for Type 1 Diabetes Associated Autoantibodies

There is a need for development of rapid, reliable, inexpensive screening tests for auto-antibodies associated with Type 1 Diabetes. The availability of such tests, which could be used in physician's offices, health clinics, and other diabetes screening settings would greatly enhance the early detection and intervention of Type 1 diabetes. Currently available methods for Type 1 Diabetes autoantibodies are time consuming and expensive, and are typically based upon radioimmuno assays. Interest is in developing assays which are simple to perform in low-tech settings and would include (but not be limited to) the following: 1) insulin autoantibody (IAA), 2) glutamic acid decarboxylase (GAD), and 3) Islet cell antibodies including *cytoplasmic islet cell antibody [ICA] 512*

D. Enhancement of blood glucose meters to improve management of diabetes

Individuals with diabetes currently use blood glucose meters to monitor short-term therapy effectiveness. However, a blood glucose measurement is simply the endpoint of a complex interplay of diet, medication, and physical activity. In order for the health care provider and the individual to make the best decisions regarding diabetes management, it is important to record all relevant data, particularly dietary intake and medication history data, affecting the fluctuation of blood glucose.

This project is for development of a hand-held device to facilitate optimal diabetes management. Improvements of the handheld device over current blood glucose meters would include the capabilities to convert food intake data into ADA diabetic exchanges and relevant therapeutic information entered by the patient such as medication and physical activity history. The device would promote better management of diabetes by facilitating compliance with diet therapy, allowing the individual to quickly record relevant factors affecting diabetes management, and the inclusion of measurement of blood glucose levels.

E. Rapid Field Tests for Vitamin A Status

There is a need for the development of rapid, rugged field portable, and economical techniques for determining vitamin A status in finger stick or ear-lobe blood samples collected by microcapillary-techniques or on filter paper. Methods may be based on fluorescence, optical density, or any other technique which reliably estimates vitamin A status in humans, but it should correlate to widely accepted "reference" methods such as high performance liquid chromatography (HPLC). Such methods would be highly valuable in global efforts to eliminate vitamin A deficiency, a high priority for WHO, UNICEF, USAID, and many other international agencies. Vitamin A deficiency is a devastating problem especially in developing countries where it contributes significantly to childhood morbidity and mortality, and is a leading cause of blindness in many parts of the world.

F. Rapid Field Tests for Iodine Levels in Urine and Salt

Iodine deficiency is a global problem affecting millions of people, leading to reduced population IQ, cretinism, goiter, and contributing to thyroid cancer. To facilitate efforts to eliminate this problem, rapid, simple, and inexpensive tests are needed that can determine the concentration of iodine in urine for population screening work, and that can determine the concentration of iodine in salt samples for quality control purposes in iodized salt production. While field tests for iodized salt have been developed in recent years, they have proven to be inaccurate and unreliable. Tests for urinary iodine

typically have required complicated laboratory procedures. Simple, reliable measures for field use would be a great help.

G. Rapid Field Tests or Continuous Monitors for Arsenic in Drinking Water

Drinking water with toxic levels of naturally occurring arsenic obtained from shallow wells is a serious problem in many parts of the world. Recently, this problem has become especially acute in rural areas of the underdeveloped world because of efforts to improve drinking water sources that unfortunately did not fully consider natural sources of arsenic. The solution requires deep wells, or water treatment at the point of use. However, because of uncertainty about the level of arsenic in water from these improved sources, and because of the need to give attention to the most heavily contaminated existing shallow wells first, there is a need to develop rapid, reliable, and cost effective tests or monitors for water arsenic.

H. Rapid Field Tests for Iron Deficiency, Iron Deficiency Anemia, and Hemochromatosis

Iron deficiency and iron deficiency anemia are serious problems throughout the developing world and in many high-risk groups in developed countries, including the United States. These problems negatively impact societies by reducing work capacity, impairing mental development and learning, and increasing morbidity and mortality, especially women of child bearing age and young children. Conversely, persons with elevated iron stores (a condition known as hemochromatosis) are at increased risk of serious health problems including cardiovascular disease, diabetes, and severe liver problems. There is a need to develop simple, reliable, easy to operate, and cost effective methods for screening for these conditions in populations and for managing individuals receiving intervention treatments. Techniques or devices which are non-invasive or minimally invasive would be most desirable.

I. Improved Tests for Zinc Status and Zinc Body-stores in Humans

The essential element zinc has been shown to be extremely important in human health. Recently it has been especially important as a co-factor in efforts to combat iron deficiency and vitamin A deficiency in the developing world. There is a need to develop simple, reliable, easy to operate, and cost effective methods for screening for zinc deficiency in populations and for managing individuals receiving intervention treatments. There is also a need for improved approaches to assessing zinc body-stores.

J. Environmental Health/Anti-Chemical Terrorism

There is a need to develop rapid, reliable, field rugged methods for detection and quantitative estimation of human exposure to environmental contaminants and toxic chemical-based weapons of mass destruction or terrorism. Such methods must be able to sense the presence or absence of such substances quickly and reliably, and provide some estimation of concentration in human urine, saliva, breath, blood, or transpired through the skin.

K. Improving Assessment of Children's Exposure to Toxic Substances

Children tend to be more susceptible to toxic substances than adults because of a variety of differences related to physical and functional characteristics. It is imperative that exposure of children to toxic substances be minimized or eliminated since exposures could result in subtle effects upon children's growth, maturation, and health. Children are generally at greater risk than adults for exposure to environmental pollutants from inhalation because they have a higher respiratory rate; from dermal exposure because they have more exposed surface area; and from ingestion because they have a tendency to play in and eat dirt.

In order to address children's exposures, the following rapid response technology is needed:

1. Development of an "environmental sensor" that would detect concentration levels of volatile organic compounds (VOCs) and particulate at threshold levels that would be harmful to small children.
2. Development of a "soil tester" that would determine the concentration

level of various trace metals and other environmental pollutants that might concentrate in soil, where children are likely to play.